THE American JOURNAL OF Surgery

MARCH 1955

THURSTON SCOTT WELTON, M.D., EDITOR

Giant-cell Tumor of Femur

The Blood Coagulation Mechanism

Bronchopulmonary Diseases—Tuberculosis

SIXTY-FOURTH YEAR OF PUBLICATION

MARCH 1955

THE American JOURNAL OF Surgery

Editor THURSTON SCOTT WELTON, *New York*
Associate Editors BRADLEY L. COLEY, *New York* · ARNOLD S. JACKSON, *Madison*
E. ERIC LARSON, *Los Angeles*

ADVISORY BOARD

LYON H. APPLEBY, *Vancouver*
CLAUDE S. BECK, *Cleveland*
H. GLENN BELL, *San Francisco*
CLARENCE J. BERNE, *Los Angeles*
B. MARDEN BLACK, *Rochester, Minn.*
GEORGE R. BRIGHTON, *New York*
MEREDITH F. CAMPBELL, *Miami*
JAMES T. CASE, *Santa Barbara*
DWIGHT E. CLARK, *Chicago*
RANDOLPH LEE CLARK, JR., *Houston*
ISIDORE COHN, *New Orleans*
FREDERICK A. COLLER, *Ann Arbor*
PAUL C. COLONNA, *Philadelphia*
GORDON S. FAHRNI, *Vancouver*
EGBERT H. FELL, *Chicago*
HERBERT C. FETT, *Brooklyn*
EMIL GOETSCH, *Brooklyn*
CHARLES A. GORDON, *Brooklyn*
DONALD GUTHRIE, *Sayre, Pa.*
Detroit, LOUIS J. HIRSCHMAN
San Francisco, EMILE F. HOLMAN
Kansas City, Mo., CLAUDE J. HUNT
New York, THOMAS J. KIRWIN
Chicago, WALTER G. MADDOCK
New Orleans, RUDOLPH MATAS
St. Louis, CARL A. MOYER
Toronto, D. W. GORDON MURRAY
San Francisco, H. C. NAFFZIGER
Baltimore, EMIL NOVAK
Christmas Cove, Me., CLARENCE R. O'CROWLEY
New Orleans, NEAL OWENS
San Francisco, VICTOR RICHARDS
Raleigh, HUBERT A. ROYSTER
Philadelphia, HENRY S. RUTH
Memphis, ROBERT L. SANDERS
Baltimore, GRANT E. WARD

AMES
COMPANY, INC.

manufacturers of *Decholin,*® *Decholin Sodium,*® *Decholin* with Belladonna, *Clinitest,*® *Acetest,*® *Ictotest,*® and other adjuncts in clinical management

announces that it has merged into its research, production and professional service programs, the facilities and products of the fifty-year old

ERNST **BISCHOFF**
COMPANY, INC., IVORYTON, CONN.

manufacturers of *My-B-Den,*® *Aminet*® *Diatussin*® and *Bi-co-tussin

*TRADEMARK

AMES COMPANY, INC · ELKHART, INDIANA

64155

Is your postoperative infection rate as low as this?

1.2 per cent infections among 6242 cases.[1]
0.9 per cent infections among 561 cases.[2]
0.6 per cent infections among 1211 cases.[1]
0.7 per cent infections among 296 cases.[1]

These results were obtained when pHisoHex was used routinely as a surgical "pre-op" hand scrub. No other scrub or wash has a *proved* record of clinical results in thousands of cases. pHisoHex is superior to all other scrubbing agents.[3-12]

pHisoHex®
(pHisoderm® plus 3% hexachlorophene)

Winthrop-Stearns INC.
New York 18, N. Y. • Windsor, Ont.

References: **1.** Bowers, R. F., in discussion of Price, P. B.: *Ann. Surg.*, 134:476, Sept., 1951. **2.** Freeman, B. S.; and Young, T. K., Jr.: *Arch. Surg.*, 61:1145, Dec., 1950. **3.** Hopper, S. H.: *Bull. Am. Soc. Hosp. Pharmacists*, 10:202, May-June, 1953. **4.** Hopper, S. H.; Beck, A. V. R.; and Wood, K. M.: *Bull. Am. Soc. Hosp. Pharmacists*, 10:199, May-June, 1953. **5.** Zintel, H. A.; Ellis, Helen; and Garcia, Martha: Paper read at the Clinical Congress of American College of Surgeons, Chicago, Ill., Oct. 5-9, 1953. **6.** Cleland, Hugh: *Canad. Med. Assn. Jour.*, 66:462, May, 1952. **7.** Harrison, Elliott; and Cockcroft, W. H.: *Canad. Med. Assn. Jour.*, 66:110, Feb., 1952. **8.** Shay, D. E.: *Oral Surg., Oral Med. & Oral Path.*, 4:355, Mar., 1951. **9.** Dennis, E. W.: Unpublished data in the files of Sterling-Winthrop Research Institute. **10.** Dull, J. A.; Zintel, H. A.; Ellis, H. L.; and Nichols, A.: *Surg., Gynec. & Obst.*, 91:100, July, 1950. **11.** Allers, Olga E.; Hubbell, J. P., Jr.; and Buck, Ann S.: *Am. Jour. Obst. & Gynec.*, 60:431, Aug., 1950. **12.** Canzonetti, A. J.; and Dalley, M. M.: *Ann. Surg.*, 135:228, Feb., 1952.

The American Journal of Surgery

CONTENTS–March 1955

VOLUME EIGHTY-NINE NUMBER THREE

EDITORIAL

Industrial Disc and Back Problem in Women . . 569

N. GILLMOR LONG, TIMOTHY A. LAMPHIER AND PHYLLIS MacNEIL

SCIENTIFIC PAPERS

"Benign" Giant-cell Tumor of Femur with Embolic Metastasis in Prepuce of Penis 573

ALFRED HAAS AND SAUL ALFRED RITTER

A report of a case of giant-cell tumor of the upper end of the femur with an isolated metastasis into the prepuce two and a half years after resection of the primary tumor.

Bile Peritonitis 579

CAPT. LUTHER G. BELL AND COMDR. HORACE D. WARDEN

The authors review the subject of bile peritonitis, giving etiology, pathology, symptoms and treatment. Three illustrative case reports are presented.

Alterations in Blood Coagulation Mechanism after Incompatible Blood Transfusion. Clinical and Experimental Observations 583

CAPT. DONALD G. McKAY, LT. COL. ROBERT M. HARDAWAY, III, LIEUT. G. H. WAHLE, JR., CPL. RICHARD EDELSTEIN AND PVT. DONALD E. TARTOCK

Contents Continued on Page 5

The American Journal of Surgery is published monthly by The American Journal of Surgery, Inc., 49 West 45th Street, New York 36, N. Y. Yearly Subscription, $15.00 U. S. A.; $16.00 Canada; $17.00 Foreign including Pan-American Countries. Single Numbers $2.00; Special Numbers $4.00. Reentered as second class matter February 7, 1951, at the Post Office, New York, N. Y., and on February 7, 1951, at York, Pa., under the Act of March 3, 1879. March, 1955—New Series, Volume 89, No. 3.

Copyright, 1955, by The American Journal of Surgery, Inc.

MANUSCRIPTS: All manuscripts should be addressed to the Editorial Office of the Journal, 49 West 45th Street, New York 36, N. Y.

Change of address must reach us one month preceding month of issue.

ADVERTISING REPRESENTATIVES

New York: P. A. Porter, P. D. Brewer and H. D. Robinson—JUdson 2-3090

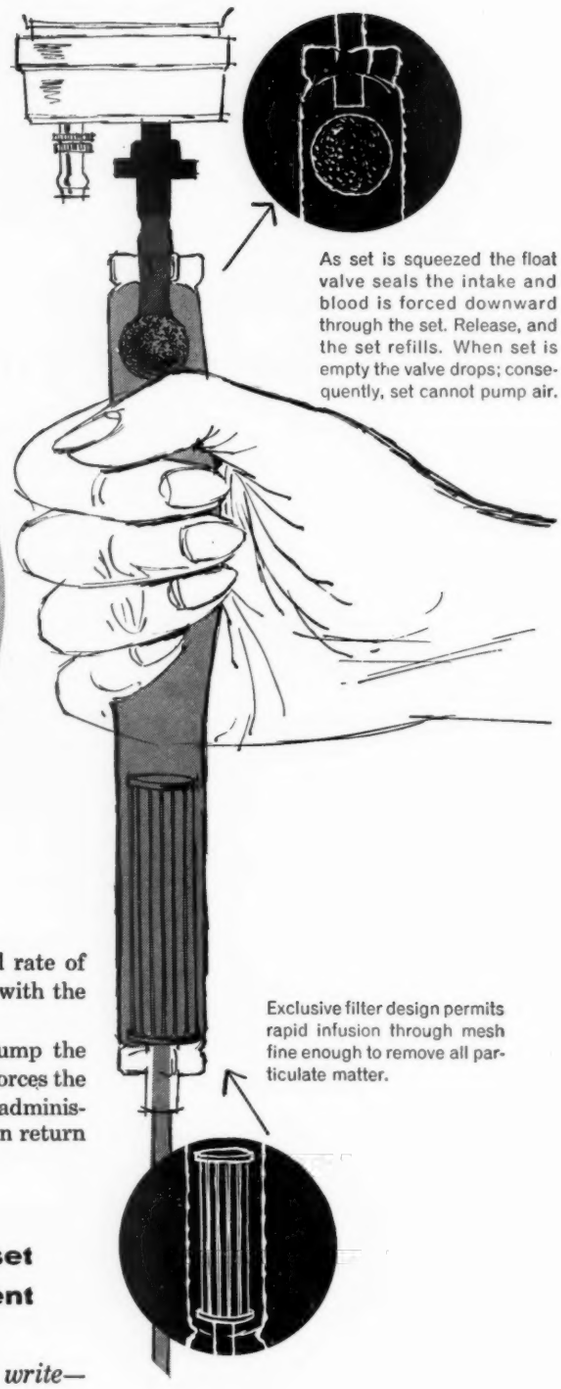
Chicago: R. H. Andrew—FRanklin 2-3861

NEW

for
administering
blood under pressure
with maximum
safety and efficiency

PLEXITRON

combination
administration set
& pressure pump



As set is squeezed the float valve seals the intake and blood is forced downward through the set. Release, and the set refills. When set is empty the valve drops; consequently, set cannot pump air.

Exclusive filter design permits rapid infusion through mesh fine enough to remove all particulate matter.

IN A FEW SECONDS you can switch from the normal rate of giving blood to rapid administration under pressure with the new Plexitron R48 Expendable Combination Set.

When the need for pressure arises you merely pump the flexible drip chamber. As it fills with blood, pumping forces the blood into the patient's veins under pressure. Rate of administration is determined by the pumping action. You can return to normal gravity administration at any time.

PLEXITRON the right set for every parenteral requirement

for sample set and complete information, write—

products of

BAXTER LABORATORIES, INC.

Morton Grove, Illinois • Cleveland, Mississippi

DISTRIBUTED AND AVAILABLE ONLY IN THE 37 STATES EAST OF THE ROCKIES (except in the city of El Paso, Texas) THROUGH

AMERICAN HOSPITAL SUPPLY CORPORATION

SCIENTIFIC PRODUCTS DIVISION — GENERAL OFFICES • EVANSTON, ILLINOIS

The authors postulate that the hemorrhagic diathesis following an incompatible blood transfusion reaction is associated with thrombocytopenia, prolongation of the coagulation and of the prothrombin time, a decrease in the circulating white blood cells, the appearance of fibrinolytic activity and of a "heparinoid" anticoagulant.

Cardiac Arrest 593

PRITCHARD T. C. LAM, JOHN T. WRZESINSKI AND BENEDICT R. WALSKE

In cardiac arrest the various prophylactic measures are emphasized. Repeated doses of atropine is believed a worth while addition to the prophylactic regimen. The various resuscitative measures are outlined. Cardiac massage is a traumatic procedure. A means of positive pressure oxygen, a knife and retractor are the only essential pieces of equipment. The urgency of immediate massage is stressed.

Evaluation of Lumbar Sympathectomy in Advanced Arteriosclerotic Peripheral Vascular Disease Complicated by Gangrene 600

LESTER L. OSTROVE

The author claims that lumbar sympathectomy will not limit the extension of gangrene in advanced arteriosclerotic peripheral vascular disease, but appears helpful in delineating the site of amputation below the knee.

Subtotal Cholecystectomy in Acute Cholecystitis . 604

GORDON F. MADDING

When feasible, total cholecystectomy is the operation of choice in the surgical treatment of acute disease of the gallbladder. When complete removal cannot be safely accomplished, subtotal cholecystectomy recommends itself. Surgical technic and illustrative case reports are presented.

New Concept of Total Hysterectomy and Anatomy of the Cervix 608

MORRIS JOSEPH

The description of a new, simplified technic for total hysterectomy which reduces the time element involved.

BRONCHOPULMONARY DISEASES—TUBERCULOSIS

Diagnosis and Treatment of Pulmonary Tuberculosis 611

ROGER S. MITCHELL

Contents Continued on Page 7

ALBUMIN THERAPY IN SHOCK

"...Serum albumin is effective in restoring lost blood volume in cases of experimental and clinical shock and behaves predictably in terms of its known osmotic and other physiochemical properties. In view of the safety, convenience and value of serum albumin as an emergency replacement fluid, in instances of severe injury or blood loss, I hope the day will come when every practicing physician will be able to carry one or two packages in his bag. The fact that the patient receiving serum albumin is safe from the risk of homologous serum hepatitis recommends it particularly as the emergency transfusion fluid of choice."

Janeway, C. A., "Clinical Status of Plasma Fractions," Int'l. Record of Med./Quarterly Rev. of Med., 168:153 (Aug. 1952).

ALBUMIN THERAPY IN CIRRHOSIS

"Intravenous use of salt-poor human albumin is no substitute for nutritional and other recognized therapeutic measures for cirrhosis of the liver. However, when judiciously used in conjunction with other treatment, it may prove to be a valuable adjuvant in the therapy of decompensated hepatic cirrhosis with ascites and edema. In selected instances it may be of crucial benefit in enabling a patient to survive a critical period..."

Portis, S. A., "Treatment of Liver Disease," Med. Clin. of No. Am., 37:1139 (1953).

ALBUMIN THERAPY IN CEREBRAL EDEMA

"...After a period of anoxia, cerebral edema often appears, for which intravenous human serum albumin seems to be an agent of choice.

"Cardiac arrest occurred during spinal anesthesia in a twenty-one year old man undergoing hernioplasty ...Cerebral (and pulmonary) edema followed... Human serum albumin was administered intravenously three times. Recovery was complete within three weeks."

Cole, Frank, "Use of Human Serum Albumin in Cerebral Edema Following Cardiac Arrest," J.A.M.A. 147:1563, (1951).

ALBUMIN THERAPY IN BURNS

"Evidence available at this time suggests that better therapeutic results might be secured if, in addition to whole blood, burn patients requiring blood replacement therapy were to be transfused with purified human serum albumin or a blood substitute suitable for albumin replacement.

"If albumin were to be administered to the system in a relatively pure form (purified normal serum albumin), it would be expected that stress on the liver would diminish and thereby reduce the fibrinogen level, with resultant improvement in the patient's condition..."

Pendergast, J. J., et al, "Albumin and Globulin Changes in Burns as Demonstrated by Electrophoresis," A.M.A. Arch. of Surg. 64:733 (1952).

ALBUMIN THERAPY IN NEPHROTIC SYNDROME

Of all types of edema none is so stubborn or so unpredictable as that associated with the chronic stages of renal disease. There is little doubt that reduced colloid osmotic pressure is an important factor in the production of this form of edema and hence albumin would appear to be the obvious physiological diuretic agent. In patients with the nephrotic syndrome, concentrated, salt-poor albumin has been successfully employed to produce diuresis.

Barness, L. A., Moll, G. H., and Janeway, C. A., "Nephrotic Syndrome," Pediatrics, 5:486 (1950).

ALBUMIN THERAPY IN HYPOPROTEINEMIA

In hypoproteinemic edema, concentrated low-salt albumin provides exactly that combination of properties needed for rational therapy. It is important to relieve edmea promptly in order to promote healing or to relieve symptoms which may be the result of hypoproteinemia.

In studies of patients with acute but reversible hypoproteinemia, the administration of albumin has elevated the level of serum albumin rapidly with diuresis even during periods of increased catabolism, when intravenous amino acids produced little benefit.[1,2]

In another study Schroeder states, "In hypoproteinemia there is excessive readsorption of salt and water by the renal tubules, leading to edema...raising plasma oncotic pressure by the intravenous injection of salt-free albumin will result in diuresis of water..."[3]

1. Janeway, C. A. Ann. Internal Med. 26:368 (1947).
2. Janeway, C. A., J.A.M.A. 126:674 (1944).
3. Schroeder, H. A., J.A.M.A., 147:1109 (1951).

6 big reasons to be sure ALBUMIN/CUTTER is readily available...

- ✓ Heat treated against hepatitis virus
- ✓ Pulls 3½ times its volume into circulatory system within 15 minutes
- ✓ Liquid, salt-poor, ready for immediate use
- ✓ No typing, grouping or cross-matching of blood required before using
- ✓ 50 cc. of Albumin is osmotically equivalent to 250 cc. of plasma
- ✓ Available in 20 cc. vials, and 50 cc. kit complete with administration set.

WRITE FOR FREE SET OF ALBUMIN FILE CARDS

ALBUMIN CUTTER

The fast-acting, hepatitis-free blood fraction

CUTTER Laboratories
BERKELEY, CALIFORNIA

CONTENTS continued–March 1955

VOLUME EIGHTY-NINE NUMBER THREE

Current Status of Antimicrobial Agents in the Treatment of Pulmonary Tuberculosis 617
NICHOLAS D. D'ESOPO

Pathology of Tuberculosis As Affected by Antibiotics 627
OSCAR AUERBACH

Mechanisms of Fatal Pulmonary Hemorrhage in Tuberculosis 637
J. ROBERT THOMPSON

Indications for Treatment of Tuberculosis in Children 645
EDITH M. LINCOLN

The Role of Resection for Pulmonary Tuberculosis in Children and Adolescents 649
MORRIS RUBIN

Surgical Treatment of Pulmonary Tuberculosis . 663
NORMAN J. WILSON, ORLANDO ARMADA, WILLIAM B. O'BRIEN AND WILLIAM V. VINDZBERG

Segmental Resection for Pulmonary Tuberculosis . 673
J. MAXWELL CHAMBERLAIN

Home Management of Pulmonary Tuberculosis and Other Forms 682
DONALD R. McKAY

Present Status of Pneumotherapy in the Management of Pulmonary Tuberculosis 687
JAMES H. CULLEN

These articles are a continuation of the Symposium featured in the January and February issues. The articles in this issue cover the subject of tuberculosis.

Contents Continued on Page 9

FOR SELF-ADMINISTERED INHALATION ANALGESIA

ACCEPTED
COUNCIL ON PHARMACY AND CHEMISTRY
AMERICAN MEDICAL ASSOCIATION

ACCEPTED
COUNCIL ON PHYSICAL MEDICINE and REHABILITATION
AMERICAN MEDICAL ASSOCIATION

Ayerst Laboratories make "Trilene" available in the United States by arrangement with Imperial Chemical (Pharmaceuticals) Limited.

"Trilene"®

Brand of trichloroethylene U.S.P. (Blue)

"Duke"® University Inhaler

No. 3160 Model-M

in obstetrics and minor surgery

notably safe and effective

"Trilene," self administered with the "Duke" University Inhaler, under proper medical supervision, provides highly effective analgesia with a relatively wide margin of safety. Induction is usually smooth and rapid with minimum or no loss of consciousness. If unconsciousness occurs, inhalation is automatically interrupted. Nausea and vomiting seldom occur. Recovery is rapid.

"Trilene" is now accepted by the Council on Pharmacy and Chemistry of the American Medical Association.

convenience of administration

The "Duke" University Inhaler (Model-M) is specially designed for economy, facility of handling, and ready control of vapor concentration. The patient treated on an ambulatory basis in the physician's office or the hospital can usually leave within 15 to 30 minutes.

The "Duke" University Inhaler is now accepted by the Council on Physical Medicine and Rehabilitation of the American Medical Association.

"Trilene" alone is recommended only for analgesia, not for anesthesia nor for the induction of anesthesia. When using "Trilene" in conjunction with anesthetic agents (as an analgesic adjunct), standard machines may be employed provided they are adjusted so that "Trilene" *is not used in a closed circuit with soda lime.* Epinephrine is contraindicated when "Trilene" is administered.

"Trilene" is available in 300 cc. containers, 15 cc. tubes, and 6 cc. ampuls.

Ayerst Laboratories • New York, N. Y. • Montreal, Canada

Ayerst

5515

CONTENTS continued–March 1955

VOLUME EIGHTY-NINE NUMBER THREE

CASE REPORTS

Hemangioendothelioma of Palate, with Wide Surgical Removal and Immediate Skin Graft 692

PINCUS SHERMAN AND CLARENCE M. CALMAN

A rare case of hemangioendothelioma of the palate is reported, with the method of surgical treatment and results one year later.

Intussusception Due to Invaginated Meckel's Diverticulum after Previous Appendectomy 696

M. C. TADDEO AND H. H. JANES

An eleven year old boy with a postoperative diagnosis of intestinal obstruction secondary to postoperative adhesions was operated upon and found to have Meckel's diverticulum with intussusception. Discussion.

Temporal Artery Aneurysm 700

WILLIAM L. MARTIN AND WILLIAM C. SHOEMAKER

Presentation of a case of temporal artery aneurysm thought to be due to arteriosclerosis.

Spontaneous Rupture of a Hydrocele Testis. . . 703

MONROE WOLF AND F. R. GOMILA, JR.

Report of a case of spontaneous rupture of a hydrocele testis with extravasation of blood into the hydrocele sac, subcutaneous tissues of the penis, scrotum, prepubic area and thighs.

Acute Appendicitis from Gunshot Trauma . . . 705

JULIEN M. GOODMAN

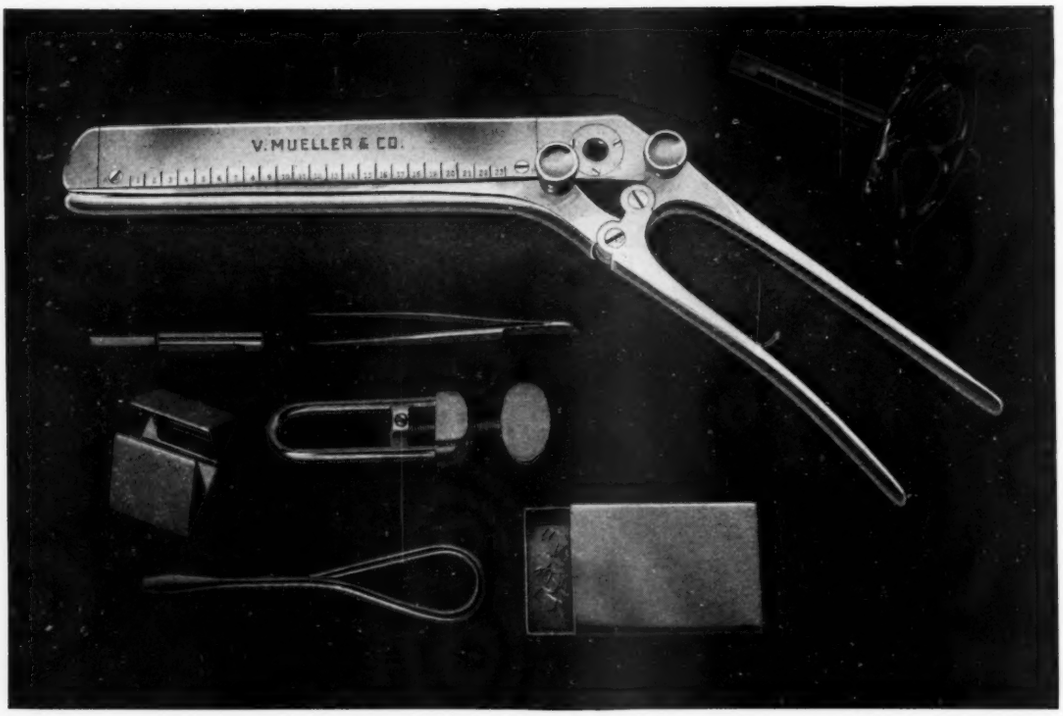
The difficulty of establishing a causal relationship between trauma and acute appendicitis is discussed and the literature briefly reviewed. A case is presented of early acute appendicitis resulting from a gunshot wound injuring the cecum but not the appendix.

Leiomyosarcoma of the Rectum 707

LT. COL. RALPH P. CAMPANALE AND MICHAEL J. CAVANAGH

A report of a case of leiomyosarcoma of the rectum (rare), a dangerous malignancy. The only hope for "cure," or arrest, is radical abdominoperineal resection.

Contents Continued on Page 11



Ingenious

is the word for this Von Petz Suturing Instrument. An invaluable time saver in stomach and intestinal surgery, this reliable device helps place the first closing sutures in deep or difficult to reach places without danger of spreading infectious contents of the stomach or intestines. It is easily handled, rapid, and sure. This particular model we have is unusually well made, with every part precisely finished and fitted for perfect performance. It is furnished in a hardwood storage case with mechanical instructions for its operation. The complete equipment includes the suture forceps and all accessories shown, and 300 nickel silver clips.

Specify MUELLER GO-2215A

Von Petz Stomach and Intestinal Suturing Apparatus, complete in case, **$295.00**

Instrument Makers To The Profession Since 1895

V. Mueller & Co.

330 SOUTH HONORE STREET CHICAGO 12, ILLINOIS

CONTENTS continued–March 1955

VOLUME EIGHTY-NINE NUMBER THREE

Omental Cyst 710

LT. COL. ROBERT M. HARDAWAY, III,
CAPT. ROBERT N. SWARTLEY AND CAPT. IRVING RUDMAN

The authors report a case of a four year old girl with an unusually large omental cyst weighing 2,600 gm. Diagnosis and operation.

NEW INSTRUMENTS

A New Non-crushing Clamp for Gastrointestinal Surgery 712

PETER K. WASKO

An Improved Sigmoidoscope for Operative Work . 714

ALFRED L. SOLOW

A New Suturing Forceps 717

F. A. L'ESPERANCE

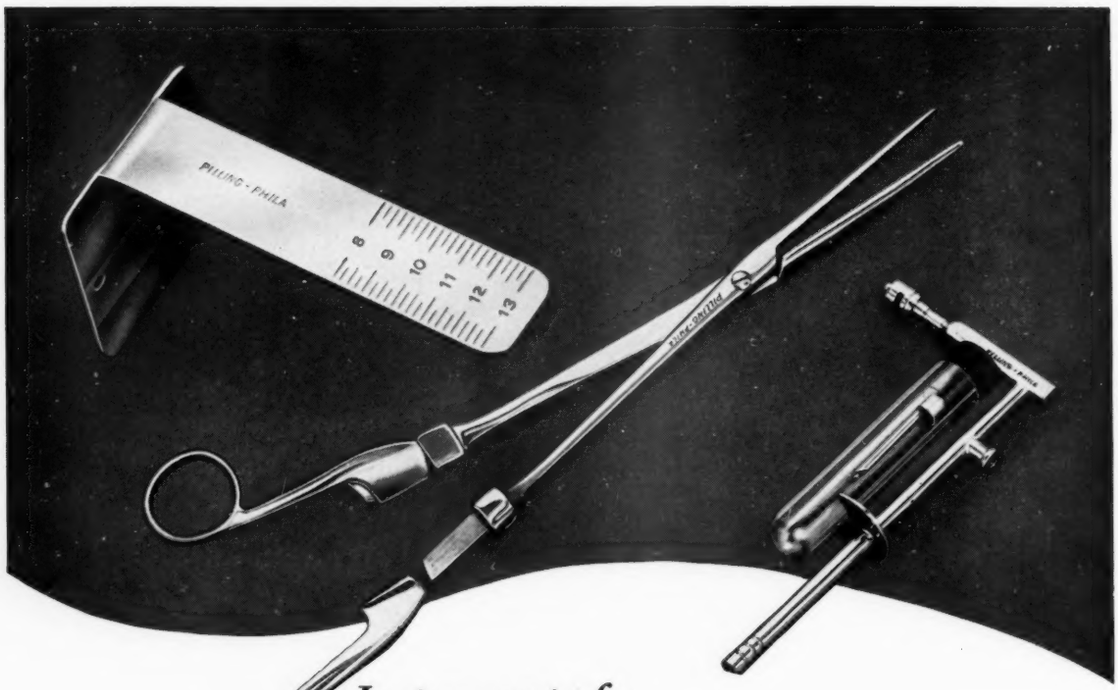
BOOK REVIEWS 718

NOTES AND QUOTES 42

* * * * *

ANNOUNCEMENT

The next meeting of the American Proctologic Society will be held June 1–4, 1955, at the Hotel Statler, New York, New York.



Instruments for

GYN *diagnosis and surgery by* Pilling

PRICE-KENNEDY VAGINAL HYSTERECTOMY CLAMPS

More Room in the Operative Field

Removable handles eliminate "rings" from operative area. Surgeon has clear view, more working space. Particularly valuable when several clamps are required. Handles are interchangeable, quickly replaced for removal.

G450 Set of two clamps, one pair handles.

BARNER SUCTION COLLECTOR FOR BIOPSIES

Attach Luer lock instruments (needle, curette, or tube) to suction tip. Collect specimen in removable bottle. Apparatus easily cleaned and sterilized, can be kept on instrument tray. Ideal for office procedure with water suction adapter. Thumb valve control.

G307 Barner Collector, one specimen bottle.

DOUGLAS MEASURING PLATE

Attach to wall, make digital measurement of internal conjugata without a pelvimeter or the help of an assistant.

G1045 Complete, with mounting screws. Stainless steel.

Pilling instruments are available only from Pilling . . . Order direct

GEORGE P. **Pilling** & SON CO.

3451 WALNUT STREET PHILADELPHIA

In this... "the Commonest Disease of Civilized Man"

- In hypertension, management can now be started in the earliest stages ... to retard progression, with the goal of prolonging useful life.

- Fully one half of all cases of mild, labile hypertension can be controlled with simple Rauwiloid therapy.

- Rauwiloid accomplishes what mere sedation cannot . . . the patient is spared the reaction to tension situations . . . without somnolence, without clouded sensorium, without change in alertness.

- The feeling of well-being engendered by Rauwiloid may become manifest as soon as 24 to 48 hours after the first dose. Its antihypertensive effect becomes apparent in two to three weeks.

- In the face of tension-producing stimuli, Rauwiloid, through its sedative and bradycrotic properties, provides tranquil equanimity.

- Its dosage schedule is uncomplicated, definite, easy to follow: Merely 2 tablets at bedtime. For maintenance, 1 tablet usually suffices. No contraindications.

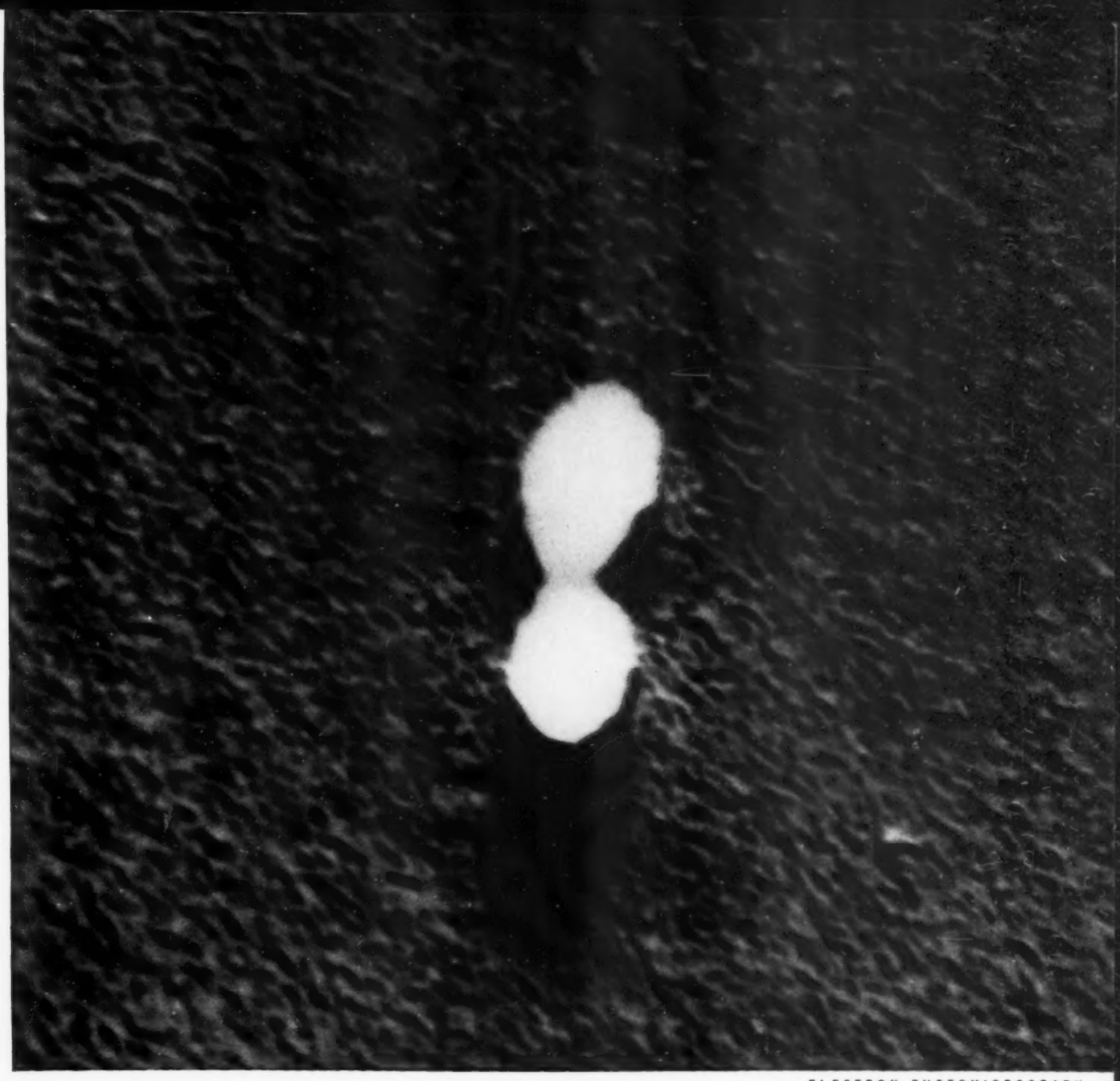
Rauwiloid® *First Thought* IN HYPERTENSION

Riker LABORATORIES, INC., LOS ANGELES 48, CALIF.

simple, effective conception control

Ortho

PRECEPTIN®
vaginal gel



ELECTRON PHOTOMICROGRAPH

Streptococcus faecalis 40,000 X

Streptococcus faecalis is a Gram-positive organism commonly involved in

a variety of pathologic conditions, including

urinary tract infections • subacute bacterial endocarditis • peritonitis

It is another of the more than 30 organisms susceptible to

PANMYCIN

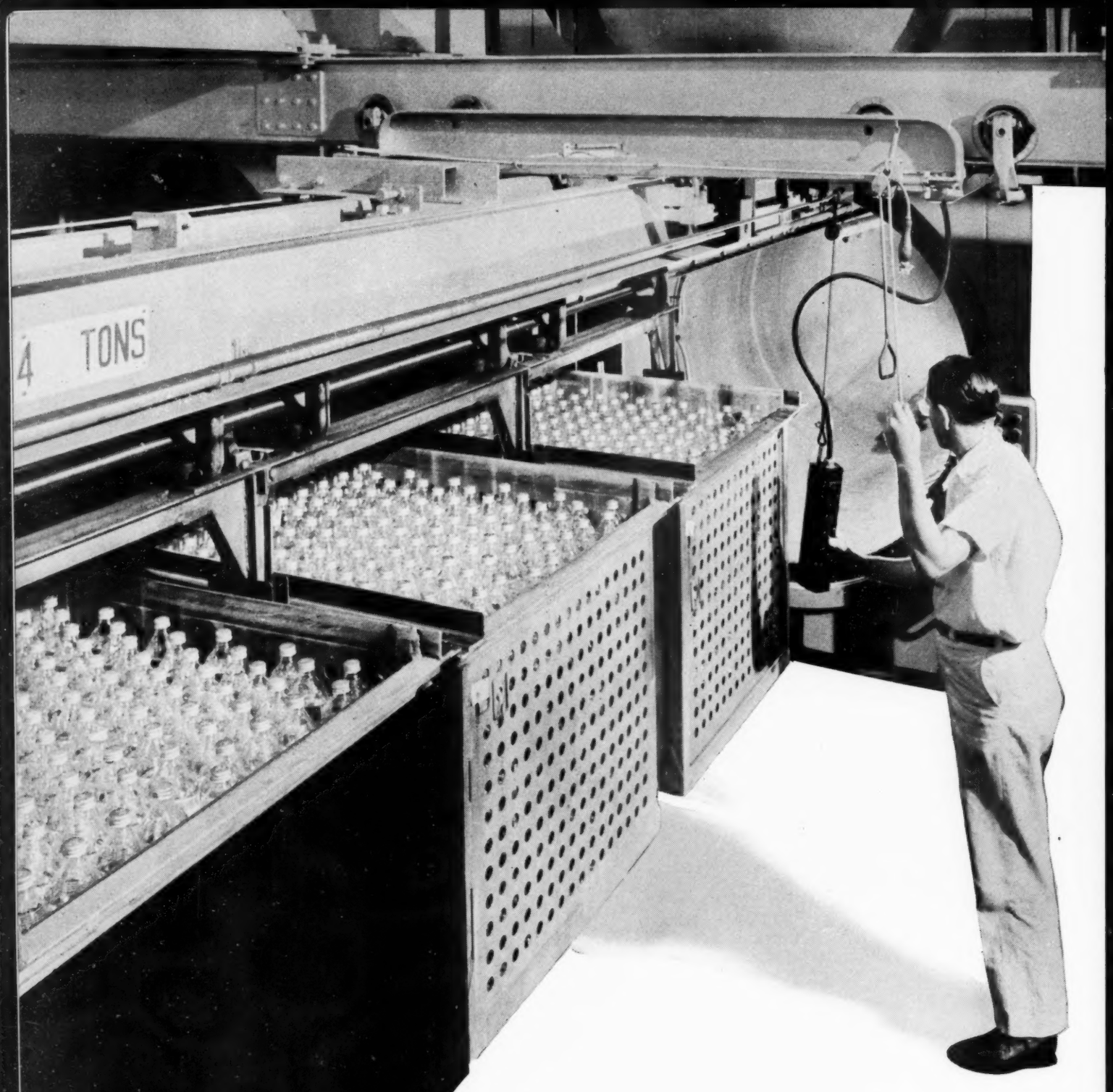
TETRACYCLINE HYDROCHLORIDE

100 mg. and 250 mg. capsules

125 mg./tsp. and 250 mg./tsp. oral suspension (**PANMYCIN** *Readimixed*)

Upjohn

●TRADEMARK, REG. U. S. PAT. OFF.

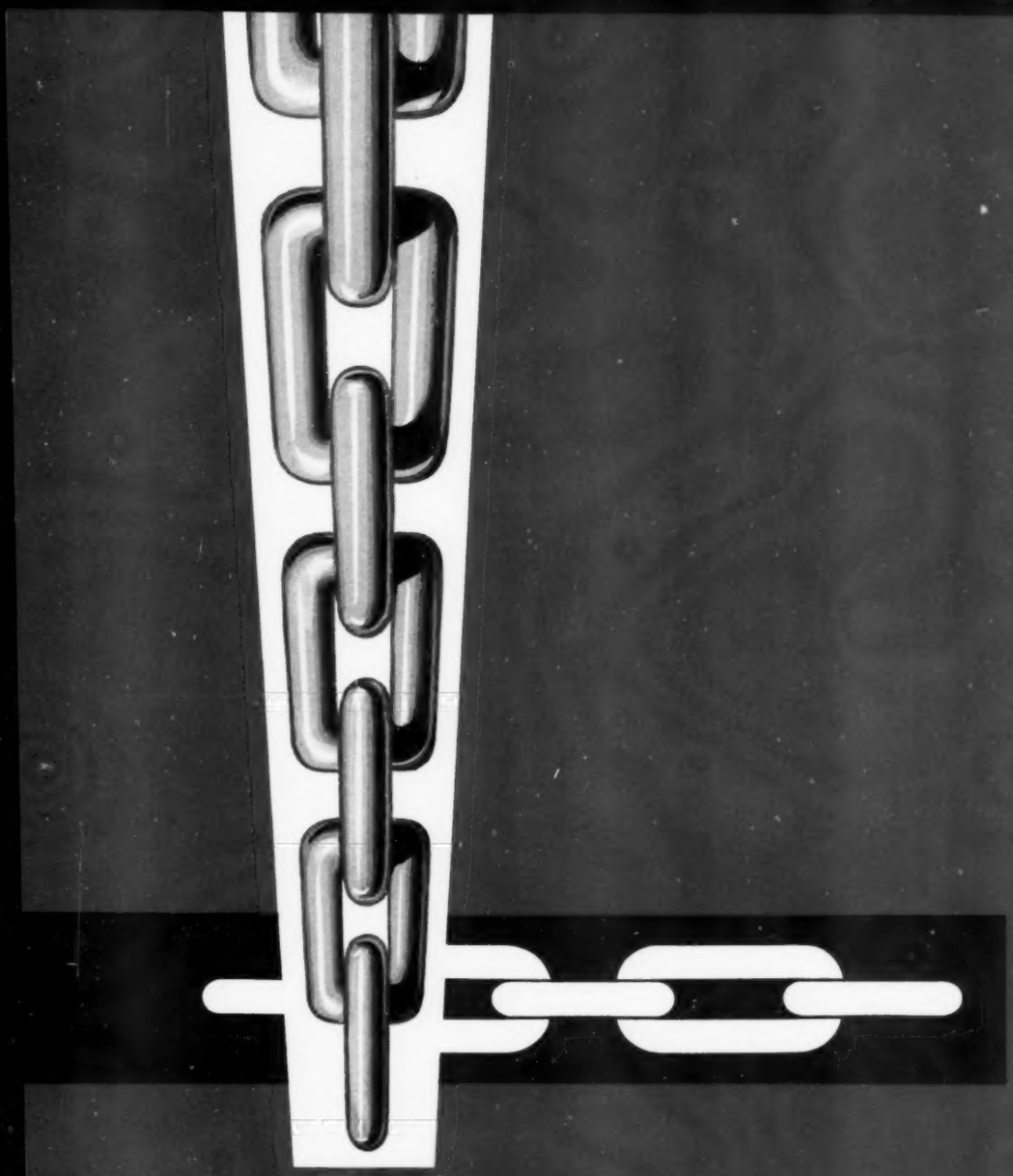


button, button

It's a comforting bit of irony that man-made machines can avoid man-made mistakes. That's why we built this giant Push-Button autoclave for our I.V. solutions. Once the pre-capped bottles are loaded in, one push of the button lowers and locks the 4½-ton door, brings up the heat, traces the temperature (even checks *inside* the bottles) and finally, measuredly cools the tunnel-like chamber down. Result? Six I.V. basketloads —thoroughly, uniformly, safely sterilized. And no mistakes.

Abbott

503099



adrenosem®

Salicylate

(brand of carbazochrome salicylate)

THE MISSING LINK IN THE CONTROL OF BLEEDING

PREOPERATIVELY • where oozing and seepage from a vascular bed is anticipated

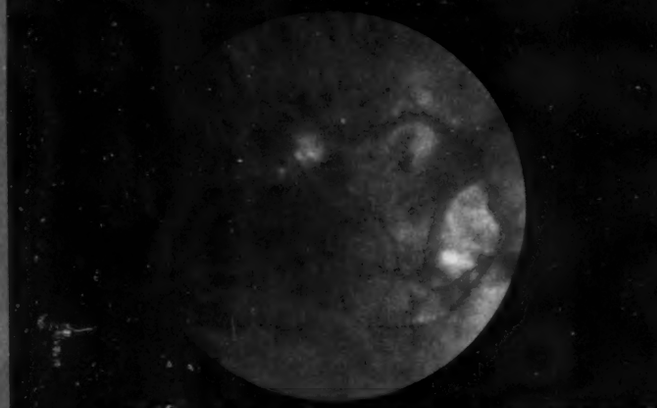
POSTOPERATIVELY • to prevent seepage and hemorrhage

TONSILLECTOMY-ADENOIDECTOMY • RETINAL HEMORRHAGE • EPISTAXIS

DENTAL SURGERY • HEMATURIA

Welling up of blood upon incision of lid and conjunctiva, common in ophthalmic procedures, hampers surgery.

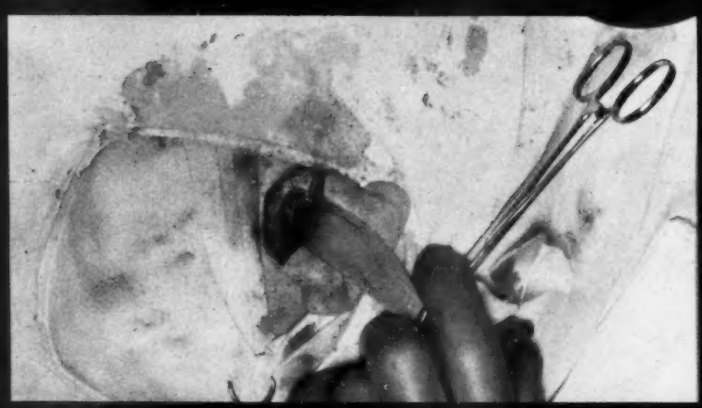
Minimal bleeding after Adrenosem therapy facilitates surgery and promotes healing.



Anticipation of recurrent hemorrhage and visual defect is high in hypertensive patients.

After Adrenosem therapy. Note exudative areas. Maintenance therapy checks further hemorrhage.

Mastoidectomy with a bloody field obscures view, requires frequent suctioning.



After Adrenosem therapy. Note clearer operative field with minimized bleeding.

Multiple extraction without Adrenosem. Note seepage. Frequent suctioning is required.

After Adrenosem therapy. Note clearer field. Minimal bleeding facilitates surgery and promotes healing.

Adrenosem®

Salicylate (*brand of carbazochrome salicylate*)

Adrenosem is specific for conditions characterized by increased capillary permeability allowing oozing and seepage bleeding. To prevent seepage bleeding due to capillary permeability it is necessary to maintain tone of the capillary wall. This is supported by Pappenheimer's[1] work on capillaries. In cases of capillary permeability it is postulated that the connective material between the cells, which form the capillary wall, has lost its tone and allows the erythrocytes to pass through.

To confirm the action of Adrenosem in establishing capillary integrity the cheek pouch of a hamster was irritated with snake venom, which has the property of making the capillaries more permeable.[2] A great many petechiae appeared on the surface and a 500 X magnification showed the capillaries with extravasation of erythrocytes. Another animal was treated with Adrenosem, and 30 minutes later, the same amount of snake venom was used to irritate the cheek pouch. Microphotographs of the same 500 X magnification show the intact capillary walls and the actual blood cells coursing through the capillaries, without signs of escaping erythrocytes.

Fig. 1—*Trauma from snake venom produces hemoconcentration and stasis, indicative of altered vascular permeability.*

Fig. 2—*Trauma does not produce petechiae following Adrenosem injection.*

Fig. 1

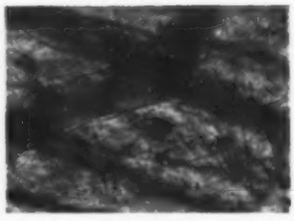


Fig. 2

Action

A systemic hemostat, Adrenosem restores capillary integrity by maintaining tone of intercellular tissue in the capillary wall. Adrenosem is unlike any hemostat available to medicine.[3,4] It does not interfere in any way with the blood clotting mechanism or its component parts. There is no sympathomimetic action and the blood pressure, cardiac rate and volume are not affected. Adrenosem may be administered simultaneously with any type of anesthetic, anticoagulant or vitamin K and heparin. Adrenosem will not interfere with the action of these agents.

THE S. E. MASSENGILL COMPANY

BRISTOL, TENNESSEE • NEW YORK • KANSAS CITY • SAN FRANCISCO

Adrenosem®

Salicylate (*brand of carbazochrome salicylate*)

BIBLIOGRAPHY

While the hemostasic action of epinephrine and related compounds has been recognized for a long time, certain characteristics limited their usefulness. A product of the metabolism of epinephrine seemed to offer the most promise. Given the name, Adrenochrome, this compound was studied extensively in both European and American centers. The handicap to wide use of Adrenochrome was its instability, so efforts were directed to find a stable modification that would retain the physiological activity. The answer to this proved to be the monosemicarbazone of Adrenochrome. Further research demonstrated that this compound could be made soluble enough to be practicable as an injectable solution, by transforming it to a sodium salicylate complex. This process has made possible Adrenosem Salicylate, a potent therapeutic agent which fills an important need in medicine.

1 *Pappenheimer, John R.: Passage of molecules through capillary walls, Physiol. Rev. 33:387-423, 1953.*

2 *Fulton, M. D., Department of Biology, Boston University: Personal communication, 1954.*

3 *Sherber, Daniel A.: Adrenochrome complex in the control of bleeding, Am. J. Surg. 86:331-335, 1953.*

4 *Roskam, J.: Arrest of Bleeding, Chas. C. Thomas, Publisher, Springfield, Ill., 1954.*

5 *Peele, J. G.: Adrenosem in the control of hemorrhage from the nose and throat (in press).*

6 *Bourgoyne, J. R. and Riddle, A. C., School of Dentistry, University of Tennessee: Personal communication, 1954.*

SUPPLY

Ampuls, 5 mg., 1 cc.: packages of 5.

Tablets, 1 mg. (s. c. orange): bottles of 50.

Tablets, 2.5 mg. (s. c. yellow): bottles of 50.

Syrup, 2.5 mg. to each 5 cc. (1 teaspoonful): 4 oz. bottles.

DOSAGE

- preoperatively to control oozing during surgery and provide clearer operative field: one to two ampuls (5 to 10 mg.) every two hours prior to surgery for two doses.
- postoperatively to prevent hemorrhage and check oozing: one to two ampuls (5 to 10 mg.) every two hours until there is no indication of undue bleeding. To maintain control, one ampul may be administered every three hours or 1 to 5 mg. orally t.i.d.
- to control active bleeding: one ampul (5 mg.) every two hours until bleeding is controlled; frequency of dose may then be diminished.
- to control mild, low-grade bleeding: one ampul (5 mg.) every three or four hours until bleeding is controlled; then 1 to 5 mg. orally four to five times daily until bleeding ceases.
- maintenance dosage to prevent bleeding in conditions where small vessel integrity may be impaired: 1 to 5 mg. orally t.i.d.; if bleeding ensues, dosage may be increased 1 to 5 mg. orally every three or four hours; if bleeding persists, oral dosage should be supplemented with one ampul (5 mg.) daily.
- pediatric dosage: up to four years of age—1 mg. intramuscularly or orally with same frequency as for adults, until bleeding is controlled. From four to twelve years of age—one-half the adult dosage as indicated.

THE S. E. MASSENGILL COMPANY

BRISTOL, TENNESSEE • NEW YORK • KANSAS CITY • SAN FRANCISCO

Detailed literature on request

NOW! RECTALGAN® AEROSOL

For Office and Hospital Use

AN OUTSTANDING ACHIEVEMENT

For Immediate Symptomatic Relief in SURFACE PAIN · BURNS · ABRASIONS · SUNBURN, etc.

Also in OBSTETRICS and GYNECOLOGY · PERINEAL SUTURING · HEMORRHOIDAL and OTHER RECTAL DISCOMFORTS

12 oz. Size RECTALGAN AEROSOL (Spray) DISPENSER

JUNIOR Aerosol (6 oz.) for Patient's R Use

Safe · Easier · Cleaner · More Efficient

Assures complete coverage of the site with this effective, quick acting, long lasting, pain relieving medication. Its use saves the valuable time of the nurse . . . gains patient cooperation and appreciation . . . assists materially in hastening recovery.

Formula:
Benzocaine 4.5%;
Carbolic Acid 1.75%;
Menthol 0.5%;
Ephedrine Alk., 0.125%-
Dissolved in Oils
(Mallon Process).

2 oz. Bottle
(with applicator)

In Obstetrics and Gynecology
Combined Therapy Proves More Beneficial

PERINEALLY	RECTALLY
Spray Aerosol over area of pathology	Instill in rectal lumen, using Rectalgan with applicator

Literature sent on request

MALLON DIVISION OF DOHO CHEMICAL CORP.
100 Varick Street, New York 13, N. Y., U. S. A.
DOHO — *Makers of* AURALGAN — O-TOS-MO-SAN — RHINALGAN

STOCKED BY EVERY WHOLESALER

broad spectrum antibiotic of choice

promptly reaches high levels in the urine

crosses the intact meningeal barrier more readily than the other broad spectrum antibiotics

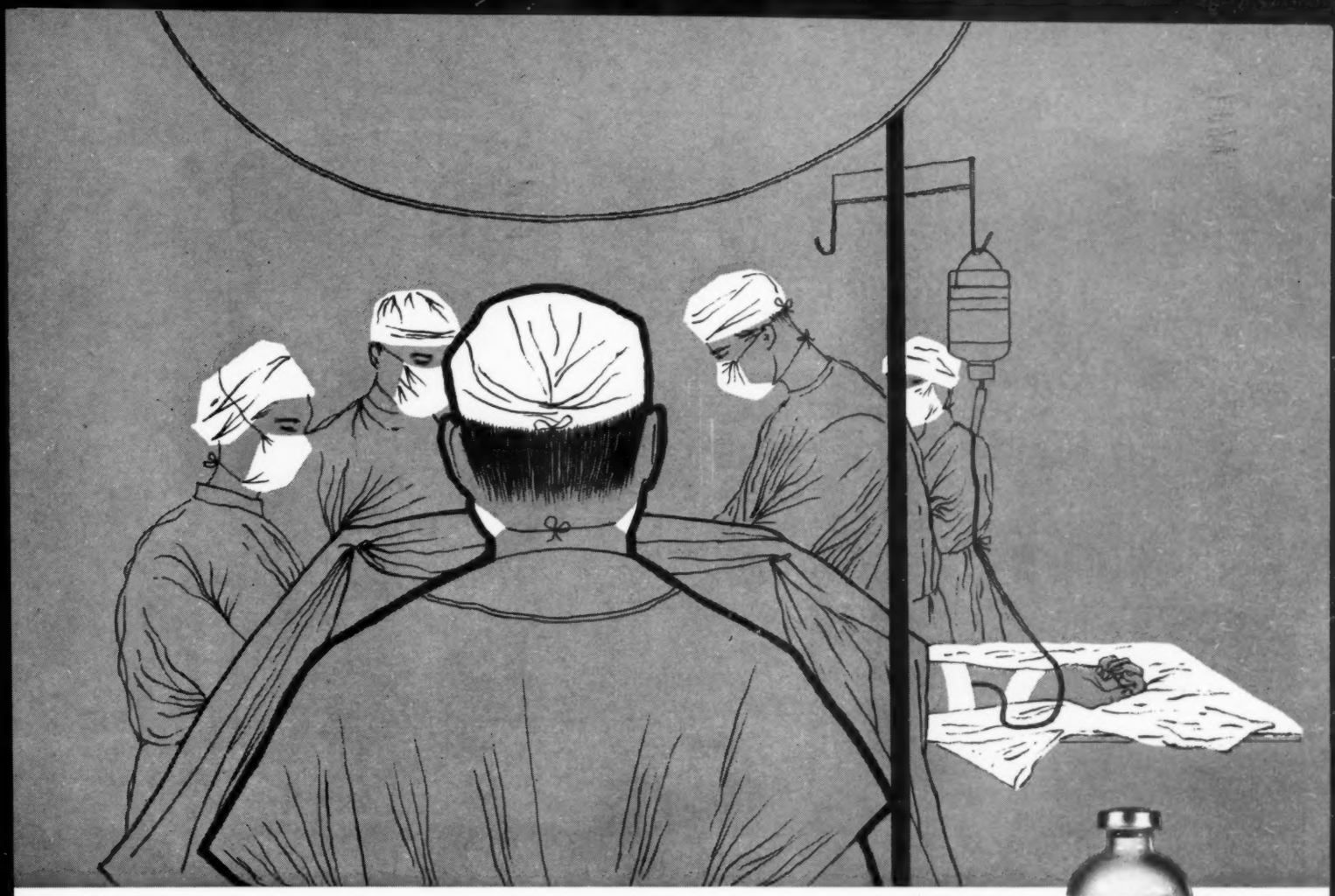
produces higher blood levels than the other broad spectrum antibiotics

less gastrointestinal side effects than the other broad spectrum antibiotics

Minimum adult dose: 250 mg. q.i.d.
250 mg. capsules, bottles of 16 and 100.
50 and 100 mg. capsules, bottles of 25 and 100.

SQUIBB

"STECLIN" IS A SQUIBB TRADEMARK



for "...smooth, rapid induction..."[1]

"...a quiet state of sleep..."[2]

"...emergence...quiet, pleasant..."[3]

SURITAL® sodium

ultrashort-acting intravenous anesthetic

SURITAL sodium (thiamylal sodium, Parke-Davis) is noted for producing smooth anesthesia with little excitement during induction or recovery. Laryngospasm is infrequent and there is relative freedom from bronchospasm and respiratory or circulatory depression.

Detailed information on SURITAL sodium is available on request.

1. Helrich, M.; Papper, E. M., & Rovenstine, E. A.: *Anesthesiology* 11:33, 1950. 2. Stephen, C. R., & Martin, R.: *North Carolina M. J.* 12:501, 1951. 3. Phillips, H. S.: *Anesth. & Analg.* 32:56, 1953.

MEDICAMENTA VERA

Parke, Davis & Company

DETROIT, MICHIGAN

Ready for you now...

Gudebrod's sutures in

DRI-PAK*

- Pre-cut lengths
- Heat sterilized by special technic
- Sealed dry in sterile tubes
- Shipped and stored in canister of sterilizing solution
- **Ready for immediate use**

Here are the finest non-absorbable sutures—dry and strong—in the most convenient hospital package. Strength and finish have been retained by use of special sterilizing technics developed especially for silk and cotton sutures.

*T.M.

AVAILABLE IN SILK:

COLOR-CODED
TRADE MARK PAT. APPLIED FOR

OR

BLACK

AVAILABLE IN COTTON:

COLOR-CODED
TRADE MARK PAT. APPLIED FOR

OR

BLUE

write for complete information

Gudebrod BROS. SILK CO., INC.

225 WEST 34th STREET · NEW YORK 1, N.Y.

PHILADELPHIA · BOSTON · CHICAGO · LOS ANGELES · DALLAS

LIVITAMIN® with IRON
each fluidounce contains:

Iron peptonized..... .....420 mg.
(Equiv. in elemental iron to 70 mg.)
Manganese citrate, soluble..... .....158 mg.
Thiamine hydrochloride..... ..... 10 mg.
Riboflavin..... ..... 10 mg.
Vitamin B_{12} (crystalline) .... 20 mcg.
Niacinamide..... ..... 50 mg.
Pyridoxine hydrochloride..... ..... 1 mg.
Pantothenic acid .... 5 mg.
Liver fraction 1..... ..... 2 Gm.
Rice bran extract..... ..... 1 Gm.
Inositol .... 30 mg.
Choline .... 60 mg.

. . . the reconstructive iron tonic of wide application . . .

LIVITAMIN®

WITH IRON

In debilitation, syndrome therapy instead of symptom treatment is required. Livitamin (Massengill) provides comprehensive therapy and adequate nutritional support. The appetite improves, as does the blood picture . . . improved anabolism and better digestion produce a significant syndrome reversal.

LIVITAMIN® CAPSULES with INTRINSIC FACTOR
each capsule contains:

Desiccated liver..... .....450 mg.
Ferrous sulfate..... .....130 mg.
(Equiv. to 25 mg. of elemental iron)
Thiamine hydrochloride..... ..... 3 mg.
Riboflavin..... ..... 3 mg.
Niacinamide..... ..... 10 mg.
Vitamin B_{12} .... 5 mcg.
Pyridoxine hydrochloride..... .....0.5 mg.
Calcium pantothenate..... ..... 2 mg.
Folic acid..... ..... 1 mg.
Intrinsic factor USP..... .....1/6 Unit

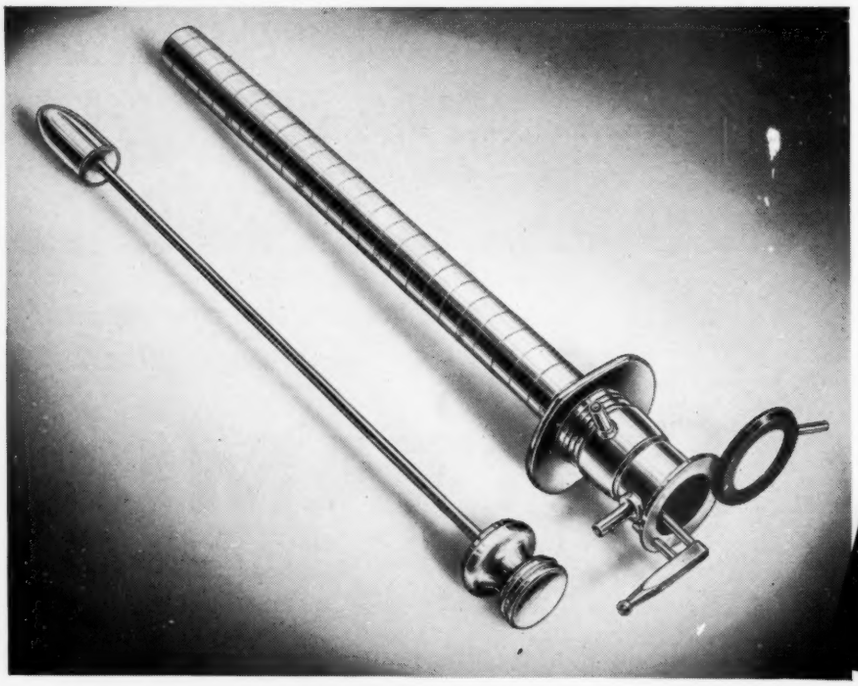
. . . in pernicious anemia and geriatrics . . .

LIVITAMIN®

CAPSULES WITH INTRINSIC FACTOR

Intrinsic factor is essential to provide full utilization of antianemic and nutritional factors in P. A. and many Geriatric patients. Livitamin Capsules with Intrinsic Factor (Massengill) contain intrinsic factor, U.S.P., iron and the B-complex vitamins. This integrated medication provides an optimal response in these difficult patients.

THE S. E. MASSENGILL COMPANY
BRISTOL, TENNESSEE



NEW

the SOLOW* SIGMOIDOSCOPE . . .
designed for simultaneous lighting

features:

- Provides extra-bright illumination of the field because proximal and distal lights function at the same time.
- When there is any distal light obscuration, the examining or operating procedure is not interrupted because . . . the proximal lamp continues to illuminate the field.
- Interruption of examining or operating procedure, because of lamp failure, is eliminated because of the dual lighting feature — either lamp alone affords sufficient illumination to carry on.
- Aspirator for evacuation of fluid or smoke is detachable thus providing the whole instrument with greater utility, more convenience.
- Speculum, of heavily chromed brass, has deeply etched calibrations at one centimeter intervals and every fifth calibration is numerically indicated at opposite sides, legibly.
- Choice is offered of plain window or one with magnification.
- Sterilizable by boiling or autoclaving.
- National catalog number . . . 450

Any "National" surgical supply dealer will be glad to show you this item, no obligation. Say: "Show me National's 450"

National

*Alfred L. Solow

NATIONAL ELECTRIC INSTRUMENT CO., INC.
ELMHURST 73, N. Y.

ELECTRON PHOTOMICROGRAPH

Escherichia coli 36,000 X

Escherichia coli ("colon bacillus") is a Gram-negative organism
commonly involved in
urinary tract infections and peritonitis,
and is an important etiologic agent of otitis media, mastoiditis, enteritis,
and septicemia in infants.

It is another of the more than 30 organisms susceptible to

PANMYCIN* HCl

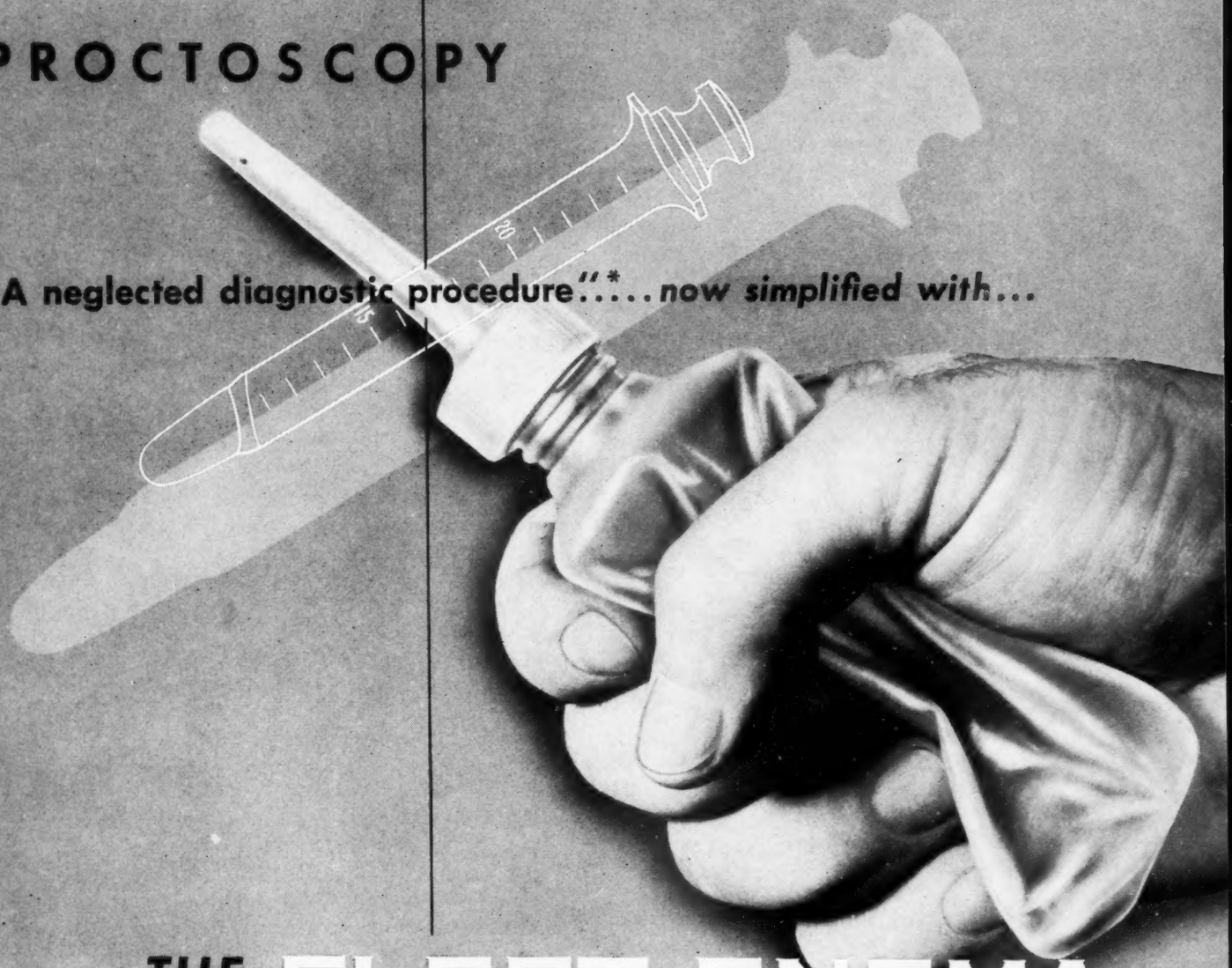
TETRACYCLINE HYDROCHLORIDE

100 mg. and 250 mg. capsules
125 mg./tsp. and 250 mg./tsp. oral suspension (Panmycin Readimixed)

*TRADEMARK, REG. U. S. PAT. OFF.

Upjohn

PROCTOSCOPY



"A neglected diagnostic procedure"*.... now simplified with...

THE FLEET ENEMA

DISPOSABLE UNIT

* ***"Probably no other office procedure except blood pressure determination in the adult gives as high a percentage of positive diagnostic information."***
— Jl. La. St. Med. Soc., 106:356, Sept. '54.

It is now a simple matter to prepare patients for proctoscopic or sigmoidoscopic examination during an office visit. The Fleet Enema *Disposable* Unit is superior in cleansing effect to a tap water or saline enema of one or two pints and less irritating than a soap suds enema. Thorough left colon catharsis, with minimal discomfort to the patient, is usually a matter of only four or five minutes.

Each 4½ fl. oz. disposable "squeeze bottle" contains, per 100 cc., 16 gm. sodium biphosphate and 6 gm. sodium phosphate . . . an enema solution of Phospho-Soda (Fleet) . . . gentle, prompt, thorough.

ACCEPTED FOR ADVERTISING IN PUBLICATIONS OF THE AMERICAN MEDICAL ASSOCIATION

"Phospho-Soda", "Fleet" and "Fleet Enema" are registered trade-marks of C. B. Fleet Co., Inc.

C. B. FLEET CO., INC. • LYNCHBURG, VA.

For prolonged

pain relief —

Levo-Dromoran Tartrate 'Roche'...a

new form of synthetic narcotic...

usually longer acting than morphine...

less likely to produce constipation...

effective in very small doses (2 to 3 mg)

...given orally or subcutaneously...

Levo-Dromoran® -- brand of levorphan.

For short-acting pain relief —

Nisentil 'Roche' usually relieves pain within five minutes after subcutaneous injection...lasts for an average of two hours... especially useful for painful office and clinic procedures... Nisentil® Hydrochloride -- brand of alphaprodine hydrochloride.

an ESTABLISHED dosage form
of choice
for PROVED broad-spectrum
antibiotic therapy

TERRAMYCIN®

Brand of oxytetracycline

INTRAMUSCULAR

the *first* broad-spectrum antibiotic
available in this convenient parenteral form
for the treatment of a wide range
of infections due to susceptible organisms.

Supplied in single-dose vials. On reconstitution,
each single dose contains: Crystalline
Terramycin hydrochloride—100 mg.
Magnesium chloride—5%
Procaine hydrochloride—2%

Pfizer

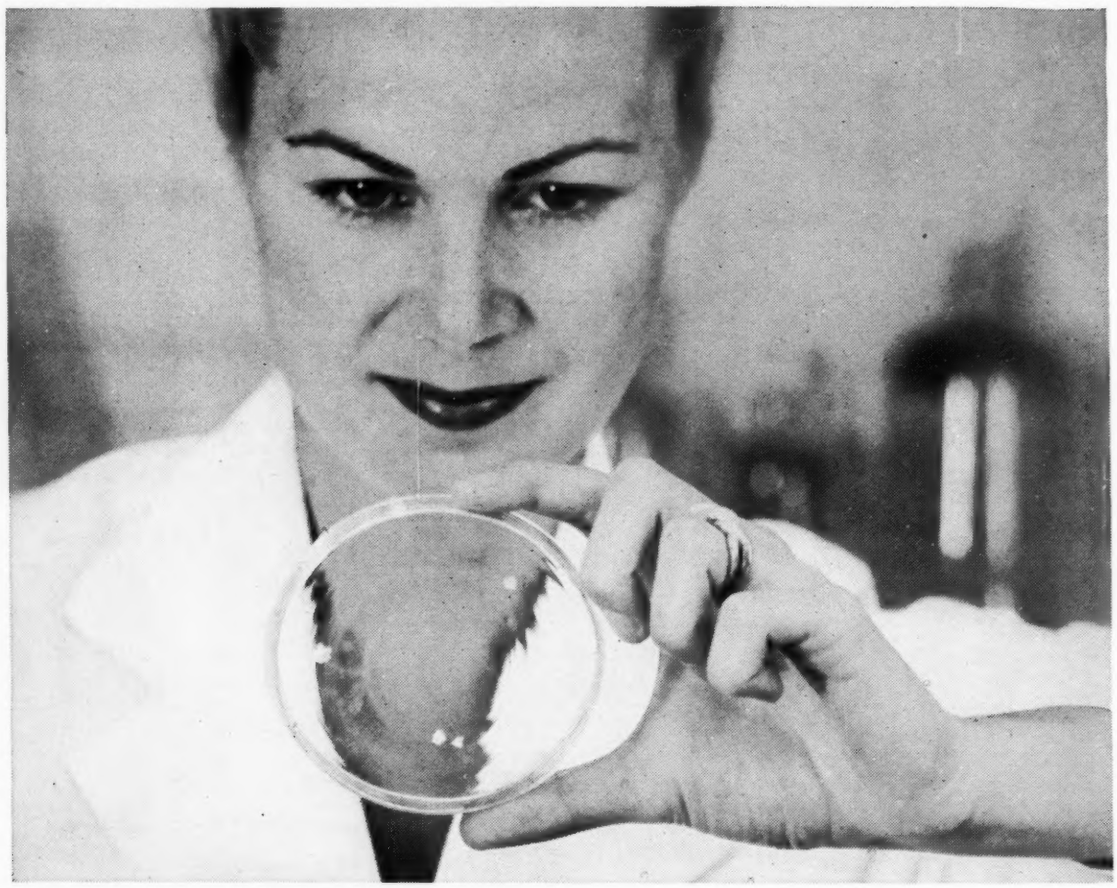
PFIZER LABORATORIES, *Brooklyn 6, N. Y.*
Division, Chas. Pfizer & Co., Inc.

Sulfathalidine®

PHTHALYLSULFATHIAZOLE

a reliably effective adjunct to intestinal surgery

MAJOR ADVANTAGES: Suppresses intestinal bacterial growth.[1] Minimum systemic absorption[2] insures maximum local effect. Effective doses well tolerated, economical.



SULFATHALIDINE, given before and after bowel surgery, is nontoxic and assures effective suppression of bacterial growth, even when there is watery diarrhea.

SULFATHALIDINE allows for preoperative mechanical preparation of the colon, favors early healing, and reduces the incidence of peritonitis. It's also a useful adjunct in ulcerative colitis. The *dosage* depends on body weight. The average adult dose of SULFATHALIDINE is 8 to 12 tablets (each 0.5 *Gm.*) daily in divided doses. 'Sulfathalidine' can also be given as the pleasantly-flavored suspension, CREMOTHALIDINE®, each oz. containing 6.0 *Gm.* of 'Sulfathalidine.'

SHARP & DOHME

Philadelphia 1, Pa.
DIVISION OF MERCK & CO., INC.

References: 1. N.N.R. 1954, p. 107. 2. Poth, E. J., J.A.M.A. *153*:1516, December 26, 1953.

Vitallium® TROCHANTERIC NAIL-PLATES

NEUFELD TYPE

NOW AVAILABLE IN RESPONSE TO THE DEMAND OF THE MANY SURGEONS WHO ASKED FOR THEM

Like all Vitallium appliances, Vitallium Trochanteric Nail-Plates are completely inert in the human body. Their strength and engineered design permits contouring at the operative site for close adaptation to the bone. They have the characteristic "satin finish" of Vitallium appliances, reducing undesirable glare during the operation.

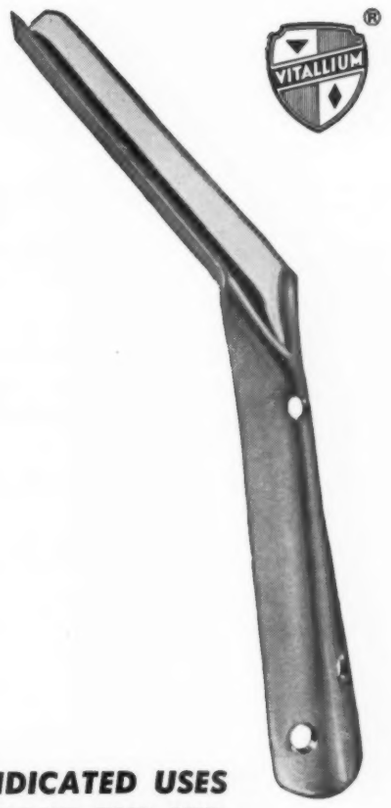
Effective fixation with Vitallium Neufeld-type nail-plates results in a feeling of security, better patient morale and shorter hospital confinement.

★ ★

Together with the Vitallium Jewett and McLaughlin-type inter-trochanteric appliances, the various Vitallium hip nails and screws, the Vitallium ready-made hip prostheses and the Bosworth-type splines, the addition of this Neufeld-type trochanteric nail-plate to the ever-increasing line of Vitallium surgical appliances provides the surgeon with a wider choice of fixation and repair appliances for the upper femoral region than is available from any other source.

★ ★

YOU CAN RELY UPON VITALLIUM SURGICAL APPLIANCES. They are made of a homogeneous, uniform alloy, completely passive, compatible and friendly to human bone and tissue.



INDICATED USES ABOUT THE HIP

1. Sub-capital fractures
2. Trans-cervical fractures
3. Per-trochanteric fractures
4. Inter-trochanteric fractures
5. Sub-trochanteric fractures
6. Oblique or spiral fractures
7. High femoral osteotomies

® By Austenal Laboratories, Inc.

ORDER THROUGH YOUR SURGICAL DEALER

AUSTENAL LABORATORIES, INC. *SURGICAL DIVISION*

224 EAST 39th STREET • NEW YORK 16, N. Y.

you can produce
prompt, prolonged
surface anesthesia
with one application of

NUPERCAINAL®

Contains Nupercaine® (dibucaine CIBA), one of the most potent and long-acting anesthetics.

Effective in low concentration —sensitization rare (nonnarcotic —not related to cocaine or procaine).

Useful whenever surface anesthesia is required—burns, surgical dressings, hemorrhoids, abrasions, etc.

Ointment (dibucaine ointment CIBA), 1% Nupercaine in lanolin and petrolatum base.

Cream (dibucaine cream CIBA), 0.5% Nupercaine in water-soluble base.

Ophthalmic Ointment, 0.5% Nupercaine in white petrolatum, applicator-tip tubes.

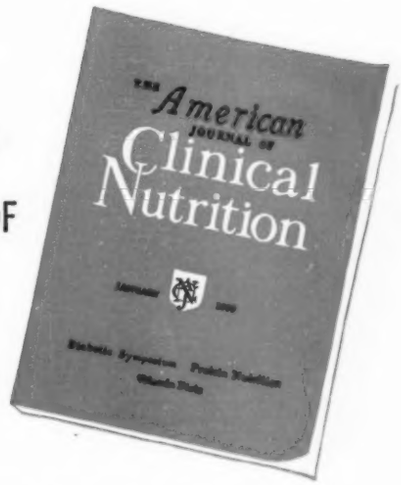
2/2091M

THE TOTAL CARE

OF EVERY PATIENT INCLUDES

PROPER NUTRITION

...AND YOUR REGULAR READERSHIP OF



NOW PUBLISHED BI-MONTHLY by your publisher of The American Journal of Surgery and The American Journal of Medicine.

Whatever your specialty in medicine or surgery, nutrition is of first importance to you in the clinical treatment and daily management of your patients. THE AMERICAN JOURNAL OF CLINICAL NUTRITION is the only periodical of its kind prepared for the doctor in practice—family physician or specialist. Within its pages are the latest data dealing with dietary problems—written authoritatively—written from the practical aspect of helping you with a newborn that is losing weight, with a middle-aged woman who is overweight, with a diabetic just admitted to surgery, and scores of other clinical cases under your management. Send your subscription *now* for this *practical* and *permanently useful* journal.

FOR PRACTICAL APPLICATION OF NEW ADVANCES IN NUTRITION BY

- OBSTETRICIAN
- PEDIATRICIAN
- INTERNIST
- SURGEON
- GERIATRICIAN
- GENERAL PHYSICIAN

THE AMERICAN JOURNAL OF CLINICAL NUTRITION

Editor-in-Chief

S. O. WAIFE, M.D., F.A.C.P., ASSOCIATE IN MEDICINE, INDIANA UNIV. MED. SCHOOL

USE THIS CONVENIENT SUBSCRIPTION ORDER FORM

THE AMERICAN JOURNAL OF CLINICAL NUTRITION
49 W. 45th Street, New York, N. Y.

Gentlemen: Kindly enter my subscription for 6 issues (one year) of THE AMERICAN JOURNAL OF CLINICAL NUTRITION AT $6.00*

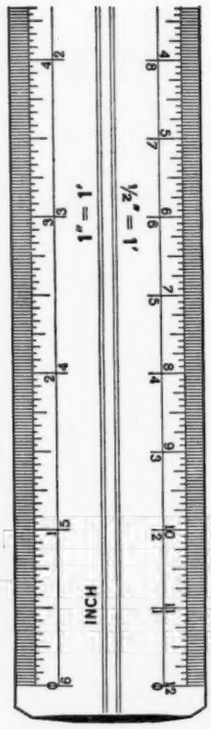
☐ I enclose remittance ☐ Please bill me

Name_____

Address_____

City_____ Zone____ State_____

*Canada, Central and South America $6.75; other foreign $7.00



by any measure it's

BARD-PARKER RIB-BACK SURGICAL BLADES

and by any measure it is just as true today as when our Company was founded . . . in the purchase of B-P RIB-BACK SURGICAL BLADES you are provided with the most dependable cutting edges that modern scientific methods and *the art of accuracy* can produce . . . their performance in use is the answer to the question of economy!

Ask your dealer

BARD-PARKER COMPANY, INC.
Danbury Connecticut, U.S.A.

ENDURING CUTTING EDGES • UNIFORMLY SHARP • QUALITY AND DEPENDABILITY •

It's Sharp

RIB-BACKS packaged in the *new* RACK-PACK eliminates unwrapping, handling or racking of individual blades. A real *time* and *labor* saver for the O.R. personnel. *In a matter of seconds* from RACK-PACK to sterilizer.

ELECTRON PHOTOMICROGRAPH

Streptococcus pyogenes 36,000 X

Streptococcus pyogenes is a Gram-positive organism commonly involved in a great variety of pathologic conditions, including

scarlet fever • tonsillitis • pharyngitis • otitis media • sinusitis
bronchopulmonary disease • pyoderma • empyema • septicemia • meningitis
mastoiditis • vaginitis • rheumatic fever • acute glomerulonephritis

It is another of the more than 30 organisms susceptible to

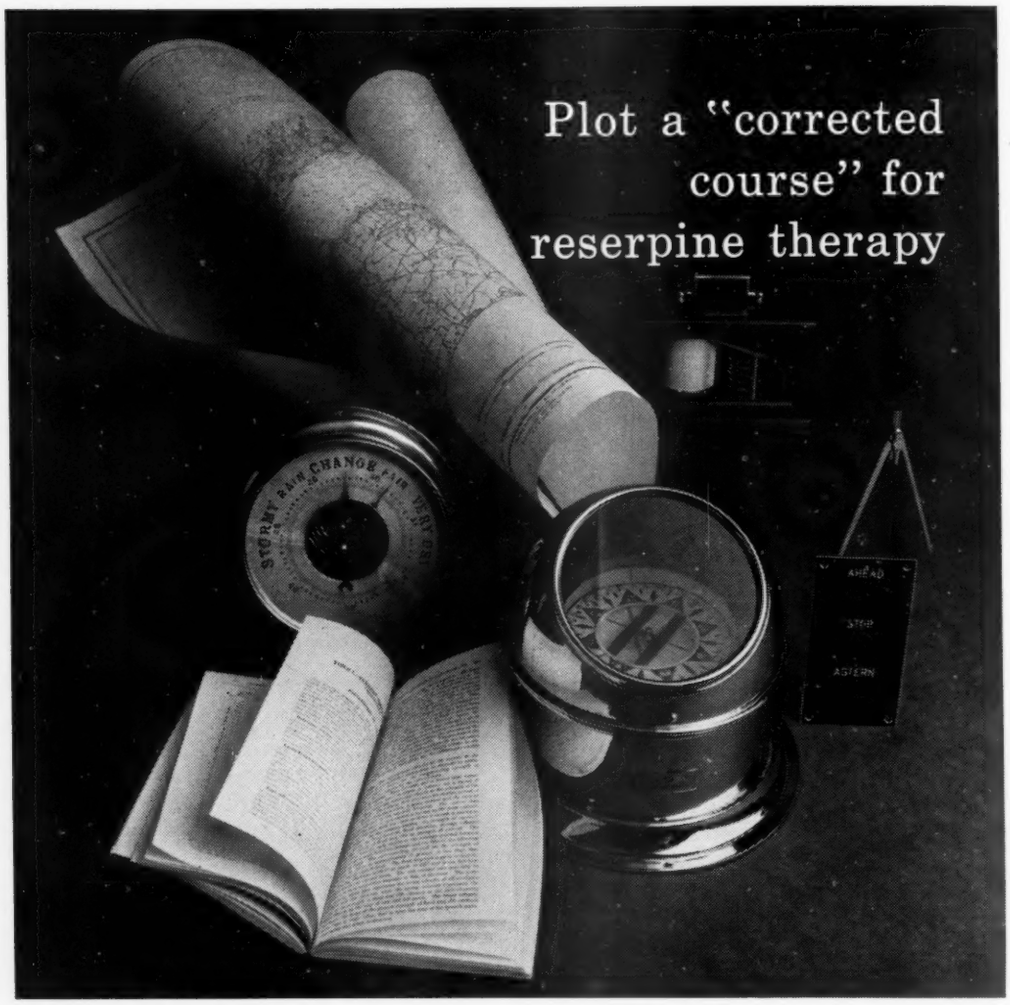
PANMYCIN* HCl

TETRACYCLINE HYDROCHLORIDE

100 mg. and 250 mg. capsules
125 mg./tsp. and 250 mg./tsp. oral suspension (Panmycin Readimixed)

Upjohn

*TRADEMARK, REG. U. S. PAT. OFF.



Approximately 50 percent of all patients taking a reserpine drug are plagued by unpleasant nasal congestion. But they needn't be!

'Sandril' c̄ 'Pyronil'

(RESERPINE, LILLY) (PYRROBUTAMINE, LILLY)

. . . offers gratifying relief from nasal stuffiness in 75 percent of patients affected by this side reaction. Of course, 'Sandril' c̄ 'Pyronil' continues to provide gradual and sustained reduction of blood pressure and to restore tranquility in anxiety states, nervousness, and the menopause.

EACH TABLET CONTAINS: 0.25 mg. 'Sandril' (for hypotensive and sedative effect)
7.5 mg. 'Pyronil' (for antihistaminic effect)

Adult dosage ranges from 1 to 4 tablets daily.
In bottles of 100 and 1,000.

Lilly

QUALITY / RESEARCH / INTEGRITY

ELI LILLY AND COMPANY • INDIANAPOLIS 6, INDIANA, U.S.A.

The American Journal of Surgery

A PRACTICAL JOURNAL BUILT ON MERIT

sixty-fourth year of publication

VOL. 89 MARCH 1955 NUMBER THREE

Editorial

INDUSTRIAL DISC AND BACK PROBLEM IN WOMEN

From an industrial standpoint back injury in women presents a problem both as to actual causative factors involved and proper treatment and disposition. Our experiences with operative cases are no different from those reported by other investigators, with our percentage figures comparable to those reported by Aitken.[1] At a recent Orthopedic Club meeting it was generally conceded that for all practical purposes the results of female industrial disc surgery was practically nil as far as return to former employment or any work requiring the usual back muscle action or expenditure of physical effort is concerned.

There is little question as to the existence of female disc lesions due to rupture of the annulus fibrosus with herniation of the nucleus pulposus following trauma. This has been summed up very well by many writers, including Bradford and Spurling[2] and Armstrong's excellent book dealing with this "recalcitrant" problem.[3] The term "sciatica" is no longer a diagnostic entity but merely a finding suggestive of nerve root irritation. It is now well recognized that loss of the patella reflexes, sensory changes, reflex changes with or without atrophy and cauda equina paralysis can be due to exudative and adhesive arachnoiditis following myelography, avulsion of the lumbodorsal aponeurosis, hypertrophy of the ligamentum flavum, abnormal mobile vertebrae and even compression of the sciatic nerve by the pyriformis muscle. Taking into consideration the fifty-seven possible varieties of backache listed by one writer, combined with the female psychic influences and temperament and the factor of compensation added to the income of the husband, there is little question as to any one surgical procedure or diagnostic approach offering a solution to the problem.

Of the 100 cases studied, the ages varied from twenty to fifty-eight years of age with disc explorations being confined largely to the forty- to fifty-year age group.

Careful analysis found no correlation of any distinct value between height and weight, the former ranging from 4 feet, 10 inches to 5 feet, 8 inches, and the latter from 94 to 200¼ pounds.

History of previous back trauma, either industrial or non-industrial, was expressed by 27 per cent. It was impossible to verify the degree or type of previous back injury in the majority of these cases, and it was of little value in drawing any relationship to the "present" trauma.

It was also very difficult to get a conclusive medical work-up, either by vaginal, genitourinary or other special examinations; but in a review of a series of 100 female back cases taken at random over a one-year period, it is doubtful that the results of special examina-

[1] AITKEN, A. P. Rupture of the intervertebral disc in industry. *Am. J. Surg.*, 84: 261, 1952.

[2] BRADFORD, F. K. and Spurling, R. G. The Intervertebral Disc. Springfield, Ill. Charles C Thomas.

[3] ARMSTRONG, J. R. Lumbar Disc Lesions. Baltimore, 1952. Williams & Wilkins Co.

tions would throw much light on the problem. All male patients over fifty have a routine rectal examination, and we have yet to encounter an appreciable number of early or late malignancies or prostatic hypertrophies worthy of note. This is not to be construed as any reason why a complete physical evaluation is not in order, for one early detected malignancy of 1,000 negative examinations is obviously worth while for diagnostic reasons. It is generally accepted that approximately one-third of all women examined by physicians show some evidence of genital prolapse, with the complaint of low backache or pelvic discomfort due to a lax perineum, lax pelvic floor, cystocele, rectocele, urethrocele or uterine prolapse. Work done at the University of Southern California showed, after 3,000 female examinations, that a great percentage of genital relaxation was due to atrophy of the pubococcygeal portion of the levator ani. How much physiologic overlay is translated into the "pain" of a ruptured disc syndrome is problematic but should be considered in any back evaluation.

There is little question that the finding of osteoarthritic changes in a woman should be followed up by sedimentation rates and antirheumatic therapy before submitting the patient for myelographic studies or explorations. Here the individual's pain threshold may be translated as a disc syndrome suspect when actually one is dealing with an arthritic back problem aggravated by an acute sprain which has long ago subsided, leaving the patient with her original early unrecognized arthritis. While it is true that one can have a disc rupture superimposed on arthritis, it is equally true that one can have spinal arthritic changes simulating a disc. Even though the figure is purely a conjecture, the x-rays reviewed showed as high as 78 per cent having early, moderate or advanced spinal and pelvic arthritic changes. The writers use the word "conjecture" advisedly as we had no way of evaluating the non-symptomatic arthritic complications.

Undoubtedly, postmenarchial disturbing influences played a great factor in many of these cases, as did other psychologic factors. Therefore it was difficult to be certain as to what degree of importance such factors bore in the individual case. The majority of cases fell into the forty- to fifty-year age group, but here again we had to work on the assumption that such psychic factors acted as aggravators rather than instigators. One of our bad cases is now under consideration for an additional exploratory operation for a missed disc, for fear of a previously missed disc. This case falls into the category described by Angyal.[4] These are the individuals who have retained their childish interpretations and premature opinions of adult problems. Certainly no scalpel is going to cure this brain phantasy with diffuse back complaints engrained deeper and deeper into unfertile gray matter by sympathy from "understanding" friends, and the frantic desperation of family doctors forced to do something for "poor Sophie's back pain."

The writers attach much importance on straight leg–raising with or without visible involuntary spasm or pelvic tilting. We have not used Bragard's test of combining this with dorsiflexion as we believe it gives a false interpretation. Only the so-called positive cases will be of interest in this respect, as well as other signs formerly thought to be of diagnostic significance. It should be noted as to where the patient complains of pain (foot, calf, thigh, gluteal region, or the back itself). Of the so-called disc cases, a positive straight leg–raising test was recorded in 89 per cent. We do not attach too much credence on the segmental representation of knee or ankle jerks, and have found in large series of cases proved at operation that no great importance could be attached to "stocking anesthesia," as the results of dermatome distribution as well as motor changes were so variable. Occasionally we ran into the textbook case, so well described by Dandy as a telephone diagnosis case, only to find that in many patients no demonstrable disc was present to offset a definite ruptured disc. We used to do the jugular compression test routinely (Naffziger) but no longer attempt it on industrial cases for obvious reasons.

History of the alleged female back injury revealed that the majority of cases were due simply to leaning over to pick up something, with no direct back blows reported, but only a twisting while lifting. The worse case we had, which ended up with a negative exploration, was a patient who incurred a coccygeal injury by falling off a chair which broke.

Most writers dealing with disc problem men-

[4] ANGYAL, A. Evasion of growth. *Am. J. Psychiat.*, 110: 1953.

tion aggravation of back and leg pain by coughing or sneezing. We are not as impressed with this syndrome as non-industrial surgeons, as we are convinced that many of the patients referred to us or sent in for direct examination come with well tailored stories. Many trite medical terms are those given to us by the patient and are not ours. We agree that a bona fide case of aggravation of back and leg pain by sneezing or coughing is highly significant if supported by other positive findings. Of the disc cases diagnosed as positive, as many as 80 per cent of the patients claimed such aggravation.

Total protein examination has been found to be of no diagnostic value and is no longer included in our routine evaluation. We much prefer to replace this test with a sedimentation rate which might suggest inflammatory or infective processes as a basis for reported back or "sciatic" pain.

False-positive myelograms, as well as the danger of such a test in contrast to discography, have been well discussed by Cloward and Buzaid.[5] We believe that there is no value in taking a myelogram unless a positive myelogram, in addition to other suggestive findings, is to be followed by operative treatment. In a high-strung, neurotic female a myelogram is not to be considered lightly, as we have had all sorts of complications from such tests. There is room for neurosurgical research in discovering a more accurate and simpler device than our present day methods. Of the 100 female back cases reviewed for this paper, thirty-two were diagnosed as positive disc cases, of which twenty-two (68.7 per cent) had positive myelograms; of this number sixteen (72.7 per cent) were operated upon with seven (44 per cent) showing no disc disorder at time of operation by competent neurosurgeons. From the thirty-two diagnosed disc cases, eight (25 per cent) returned to work; of the operative exploratory cases (sixteen) one returned to work in fourteen months' time; the other fifteen patients are either on compensation or have received full settlement.

The remaining sixty-eight cases were classified as acute back sprains and treated as such, with individual cases of fibrositis,[6] myositis and the like included in this group. The shortest period of treatment of the typical female low back sprain was four days and the longest over two years, the latter case being a bit unusual with all tests, consultations and evaluations failing to show any positive disc disorder. Patients who were definitely osteoarthritic or who had female genital causations for secondary back pain were not included in this group. Hospital bedrest, board under the mattress, daily physiotherapy and practical psychotherapy were sufficient for the majority of these patients. However, because of "education" on the part of friends who knew someone who had similar trouble which later turned out to be a "disc," many simple back problems became complex ones. Again we reiterate that we do not disregard the possibility of an existing herniated disc with each back case, no matter how trivial. We do realize that, based on a large number of cases, the solution apparently is not in the form of neurosurgery, at least at present.

In summary, this paper is written to show the unsatisfactory results of female industrial disc surgery once the label of a ruptured disc or fractured disc has been given to a female patient's condition following, very often, a trivial back incident. Not all of the thirty-two patients with positive disc cases would submit to myelographic study. All of the patients with low back sprains treated as such eventually returned to work following conservative back therapy. Whenever possible we advise a two- to three-week hospitalization in treating an acute condition of the back with visible spasm. Our results following the use of leg traction, pelvic traction, oil in anesthesia and bedrest have been comparable with those in our male patients. Psychotherapy is important, perhaps more so with the female back. Careful elimination of other physical complications is as important in this problem as any other surgical problem. The result as far as the female patient's return to industry has been nearly zero, and our results, or lack of results, are substantiated by other industrial clinics or workers. This should not imply that the poor result is due to faulty diagnosis or technic (these of course have a direct bearing as excessive, uncontrolled bleeding causes cicatricial contractures), but rather seems to center about a psychologic factor. The fact that the majority of disc exploratories are done at the

[5] Cloward, R. B. and Buzaid, L. L. Discography. *Am. J. Roentgenol.*, 68: 552, 1952.

[6] Long, N. G. and Lamphier, T. A. Fibrositis and the disc syndrome. *Am. J. Surg.*, 86: 414, 1953.

menopausal age may have a definite effect as to results. Perhaps many cases represent "evasion of growth,"[4] unrecognized until the patient falls into that category of the unsuccessful disc case. Possibly it might be a good rule to have a preoperative psychic evaluation, for we are certain many cases have a good mechanical result offset by a desire for "compensation retirement," or are complicated by some social frustration. Those of us seeing large numbers of disc cases in both men and women often wonder what happens two or three years after settlement, and whether a reasonable sum set up by State Statutory Limitations is the answer to the "back in industry," particularly in regard to women.

N. GILLMOR LONG, M.D.,
Chicago, Illinois,
TIMOTHY A. LAMPHIER, M.D.,
Boston, Massachusetts AND
PHYLLIS MACNEIL, M.D.,
Boston, Massachusetts

"Benign" Giant-cell Tumor of Femur with Embolic Metastasis in Prepuce of Penis

ALFRED HAAS, M.D. AND SAUL ALFRED RITTER, M.D., *New York, New York*

GIANT-CELL tumor was first described in 1818 by Astley Cooper and was subsequently outlined classically by Paget in 1853 and by Nélaton in 1860. It is an osteolytic lesion which has been in the foreground of interest in recent years. There are good reasons for this fact. It is difficult and not always possible to give a definite opinion about the prognosis in these cases, even with cooperation of surgeon and pathologist, notwithstanding the special experience of the latter.

Progress has been made by the intensive study of the micropathology of giant-cell tumors. Jaffe, Lichtenstein and Portis[1] have classified these tumors into three grades according to the micropathology of the stroma cells. These stroma cells are spindle-shaped and ovoid. The aggressive tumor was placed in the second grade while the third group was classified as being frankly sarcomatous.

Meyerding[2] in 1945 reviewed forty cases from the Mayo Clinic and tried to draw prognostic conclusions from the size of the giant cells. He believes that the smaller these cells are, the greater is their activity, their immaturity and invasiveness. He found a significant difference in the average number of nuclei of the giant-cell tumors in patients who had a recurrence as compared with those who recovered without recurrence. Only the future will reveal whether this fact is of practical value.

It is difficult for the individual surgeon and pathologist to gather enough experience, as these cases are rare.

According to Sir Harry Platt,[3] giant-cell tumor is a rare occurrence. Only about one case is seen each year per hospital in England. For this reason Lichtenstein[4] thinks it may be profitable for a number of hospitals to set up a giant-cell tumor registry. Pooling these cases would give more experience in order to establish more accurate diagnosis and help to standardize therapeutic procedures. Thorough follow-up studies are also advisable.

These cases can cause anxiety for the surgeon in making the decision of how to treat the individual case. We should be able to establish with some certainty the prognosis. Therefore every case deviating from the anticipated course should be brought to the knowledge of the profession. The following is the case history of our patient:

L. F. (born November 27, 1917), a white married man, was first seen on October 14, 1950, with the following history:

In January, 1950, he felt pain in the right hip. He had some orthopedic treatment and was told to use crutches to prevent weight-bearing on the right lower extremity. He was told by his orthopedist that needle biopsy had revealed a benign lesion of the right hip. He continued to have a great deal of pain, particularly at night. He had never been previously sick. Otherwise the past history is irrelevant.

The patient was 76 inches in height and weighed 182 pounds. On examination his pupils reacted to light and accommodation. The lungs were clear. The heart was regular with normal sounds, rate 84. The blood pressure was 130/80. On examination the abdomen showed no abnormality and there were no abnormal neurologic findings.

The patient walked on crutches to avoid weight-bearing on his right lower limb because of pain. The right hip was tender on pressure and very painful on motion.

FIG. 1. X-ray shows the destruction of a good deal of bone at the head and neck of the right femur and the outline of the tumor.

The right hip joint was fixed by a muscular reflex spasm in 30 degrees flexion and 10 degrees adduction. There was no further active or passive motion in the hip joint. Any attempt to move the hip further made the patient squirm and scream.

Laboratory findings were as follows: The urine was negative for sugar and albumin. Complete blood count: hemoglobin 104 per cent, red blood count 5,270,000, white blood count 5,200, lymphocytes 23, polymorphonuclears 68, monocytes 7 per cent and eosinophils 2 per cent. Sedimentation rate was 29 mm. in one hour. Alkaline phosphatase was 4.1 units and acid phosphatase 1.0 units.

X-ray of the right hip joint taken on October 26th revealed an extensive destructive rarefying lesion involving the head and neck of the femur. The outline of the defect appeared to be smooth and regular. Inside the lesion trabeculae of greater density were visible, demarcating irregular compartments. (Fig. 1.)

Routine examination of the remaining portions of the skeletal system, skull, spine, ribs, etc., failed to demonstrate any other lesion. X-ray examination of the chest revealed no abnormality. Roentgen diagnosis was giant-cell tumor.

On October 30th operation was performed from a posterior approach, question-mark incision, with reflection of the musculus gluteus maximus. At exposure it was found that the femoral neck and the head were transformed into a distended mass with a very thin shell of bone. There was a small opening at the neck in its upper part, apparently where the previous biopsy had been performed. There was an infraction of the bone at the intertrochanteric line. The already existing opening was enlarged with a small chisel and masses of tumor tissue became visible. The masses were dark blue in color. The tumor tissue was under pressure and a part of it extruded.

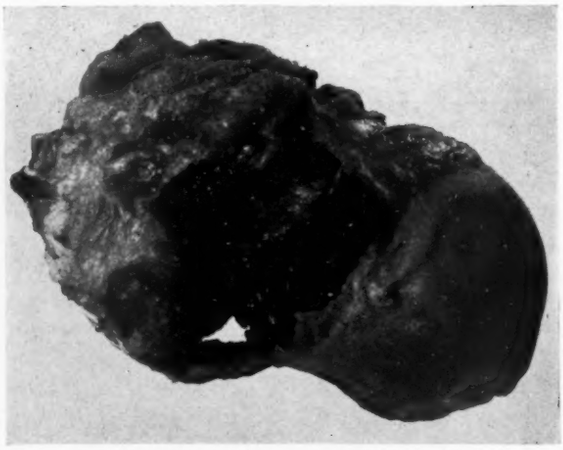


FIG. 2. Resected specimen consisting of head and neck of right femur. At the opened neck the tumor masses are visible.

Drs. Jaffe and Paltauf examined the tissue at once and concurred in the diagnosis of benign giant-cell tumor. Dr. Jaffe stated that there was danger of local recurrence unless the mass was completely removed.

The femoral head and neck were completely excised just below the lesion. The major trochanter in its outer part was found to be uninvolved. The muscular insertions were therefore preserved. The shaft was then placed into the acetabulum. The capsule of the joint and the small muscle insertions at the femur were removed. No alloplastic replacement of head and neck of femur was considered desirable in order to avoid irritating the tissues. When the small muscles in the region of the sciatic nerve were excised, we exposed the internal pudendal artery. Several of its smaller branches were cut and ligated. The wound was closed after reconstruction of the gluteus muscle. A spica cast was applied to the extremity. Figure 2 shows the removed part of the femur.

The postoperative course was uneventful; the patient recovered and was discharged from the Misericordia Hospital on December 14, 1950.

In the beginning of January, 1951, the patient was supplied with a portable splint of the Hessing type which maintained the abduction of the shaft of the femur. He walked very well and went back to work on February 19, 1951. It was reported that he was able to drive a car. He could abduct his femur 20 degrees and flex it in the hip 90 degrees. He had complete range of motion in the knee and ankle joints.

The patient was seen for subsequent checkups and was very cooperative in helping his rehabilitation. He developed his right quadriceps muscle to equal the left one, and from the beginning of 1952 he no longer wore his brace and was able to walk well without any mechanical aid. There was a very slight "Trendelenburg phenomenon."

Figure 3 shows the hip three and a half years after operation. The shaft was in good relation to the acetabulum and no recurrence of the tumor was seen.

The patient remained well until May, 1953, when he noticed the development of a small, painless nodule in the dorsal part of the prepuce. This nodule resembled a sebaceous cyst, was discrete, the size of a cherry and movable.

The tumor was excised with a piece of the prepuce under local anesthesia.

On gross section it was solid and encapsulated. Pathologic examination, however, showed it to be a giant-cell tumor of the same type which he had had removed two and a half years before from the right hip.

Because of the presence of a metastatic tumor in the prepuce two and a half years after the removal of the primary "benign" giant-cell tumor from the upper epiphysis of the right femur, deep roentgen ray therapy to the sites of the primary and metastatic lesions was instituted.

This was a surprise after Drs. Jaffe and Paltauf of New York City had concurred in the opinion that the primary tumor showed the histologic pattern of benign giant-cell tumor of bone.

The tumor, shown on the microphotograph, was composed of large, multinucleated giant cells. The stroma cells were small or medium in size, oval- and spindle-shaped, growing diffusely and held together by a loose fibrillar matrix as shown on the microphotographs. (Figs. 4 and 5.)

FIG. 3. Shaft of the femur at the upper margin of the acetabulum.

Dr. Julius Pincus of New York City examined the preputial metastasis. He recognized the same microscopic pattern present in the primary lesion of the right femur.

Dr. Arthur Purdy Stout, who reviewed the slides at a later date, made the following points: "Tumor cells are found in blood vessels. At the periphery the tumor invades the marrow spaces; bone trabeculae are destroyed by tumor.

"In the tumor of the prepuce, composed of fairly large giant cells in very cellular vascular stroma the stromal cells show frequent mitotic figures." His diagnosis was therefore osteogenic sarcoma of femur, secondary osteogenic sarcoma in prepuce.

Dr. Karl Neubuerger of Denver, Colorado, also reviewed the slides. He reported that in his opinion and those of his associates it is extremely difficult to distinguish histologically between benign and malignant giant-cell tumor. The presence of necrotic areas as we see them in the bone slides is not incompatible with this diagnosis. On the other hand he believes, just as pointed out by Dr. Stout, that invasion of the marrow cavity certainly is not one of the usual features of benign giant-cell tumor. This, as well as the presence of neo-

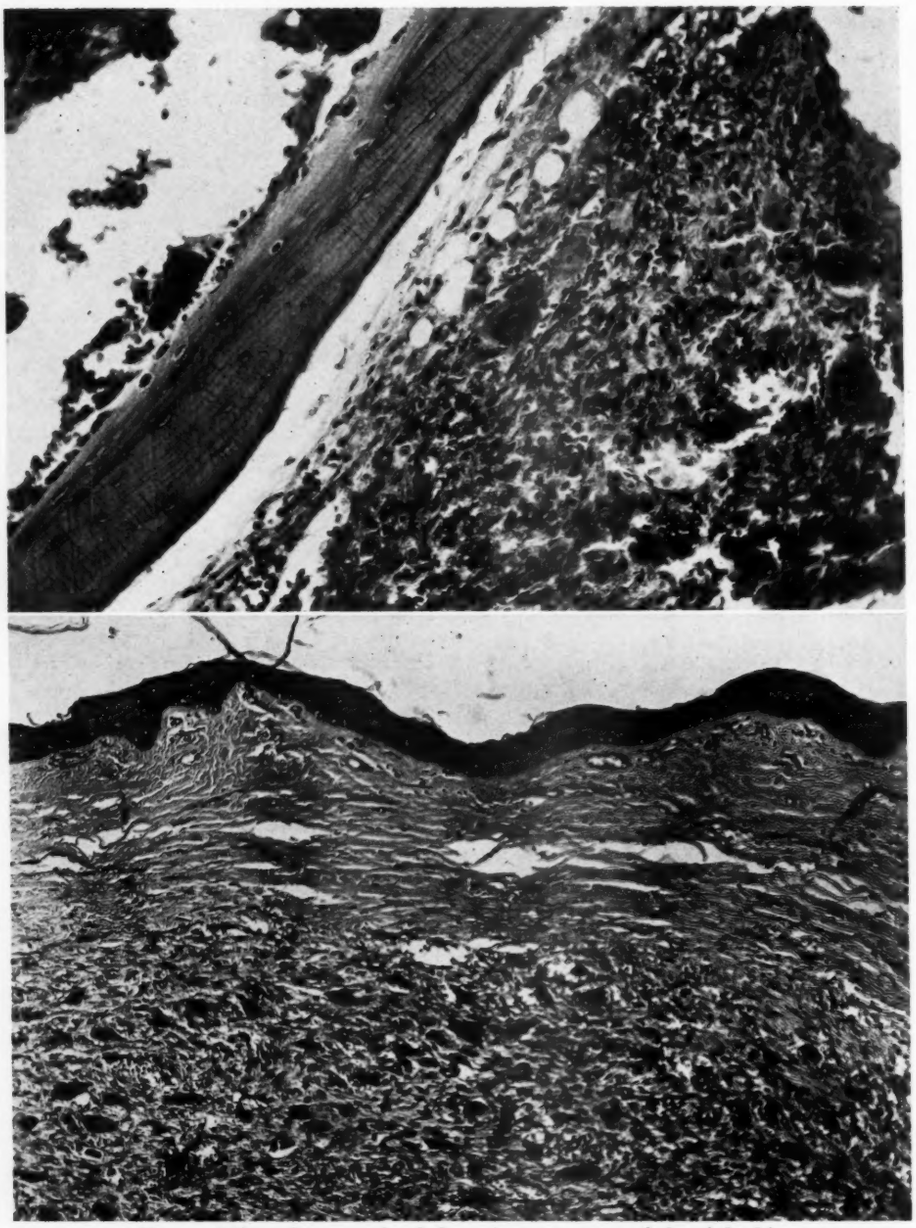


FIG. 4. Microphotograph of the primary tumor of the right hip.

FIG. 5. Microphotograph of the preputial lesion.

plastic tissue in the walls of veins with invasion of the lumen, would appear to justify the diagnosis of malignancy. He states that he has never seen marrow destruction and venous involvement in the usual run of giant-cell tumor. However, he does not believe that this tumor should be classified as osteogenic or osteolytic sarcoma because of the histologic pattern which is quite different from osteogenic sarcoma.

The metastatic lesion which occurred here after the excision of the tumor from the right femur was observed and removed after an interval of two and a half years. This metastasis can be explained only by an arterial embolism from the internal pudendal artery, as it does not seem likely to have occurred through the venous or lymphatic circulation. Why and where it was dormant for so long, whether in an arterial branch or at the site of the embolism, is a matter for conjecture.

Can we call this giant-cell tumor a malignant one? In 1934 Hotz[5] wrote that we are in need of absolutely safe criteria for malignancy or

benignity in these tumors. He and Hellner[6] find some analogy with other tumors, i.e., the microfollicular adenoma of the thyroid. This malignant adenoma frequently has a protracted course and metastasizes. The metastatic tumors grow slowly and sometimes the course spreads over a period of from thirteen to eighteen years, as one of us described years ago.[7]

The tendency to recur exists in all giant-cell tumors. The recurrence may be the same type or the microscopic structures may change into outspoken sarcoma. Local recurrence is no criterion for malignancy.

Geschickter and Copeland[8] demonstrate all the points of confusion which still exist in the microscopic diagnosis and prognosis. They stress how the microscopic picture may be changed by infection, necrosis, partial healing processes and irradiation. They say that malignancy in recurrent tumors is usually the "result" and not the "cause" of recurrence.

These authors report on eight metastasizing cases representing their group of 500 cases from the clinics of New York, Philadelphia, Chicago, Baltimore, Canada and England. They stress that typical giant-cell tumor has never been found in the lungs. When such a tumor with the original diagnosis of giant-cell tumor metastasized to the lung, the histology was osteogenic sarcoma.

Willis[9] believes that histologic distinction between the giant-cell tumor which takes the normal harmless course and those which later metastasize is difficult and perhaps impossible to make. He mentions one case which resembles our case, with a hemic metastasis in the scalp published by Dyke in 1931. All the transitions in the theory of tumors have become so vague and fluent since we now know that even in endometrioma tumor cells are found in vessels and in lymphatics. This fact proves that histology alone cannot be used as the crucial test for prognosis.

It is now one year since the metastasis was removed. The patient is in good condition and there are no signs of further recurrence at present.

COMMENTS

Apparently these tumors form a group with unusual qualities, which may be due to their connection with bone development.

In their clinical course, as in many bone tumors, there may be a history of trauma. The swelling, pain on weight-bearing or pressure are constant; deformity and functio laesa in the involved joint are typical. Night pain is not as severe as in sarcoma, but it is present. There is general agreement now that patients in the third and fourth decades of life have to be particularly evaluated, as in this age group cases with the tendency for recurrence or metastases occur. This has been stressed recently by Steward and Richardson.[10] The ratio of male to female is 1 : 1.

Generally speaking the diagnosis should be made not only on the clinical findings, but also on x-rays and biopsy.

The x-ray in giant-cell tumor shows an osteolytic lesion which usually involves one epiphyseal region in the long bones. At the femur it is more common in the lower than in the upper epiphysis. The lesion can usually be well differentiated from other lesions. The outline of the defect is usually smooth and regular. The inside shows trabeculae which subdivide the osteolytic cavity into usually irregular-sized compartments. It has been said that the fewer trabeculae found on the x-ray and the more homogeneous the defect looks, the more probability for malignant giant-cell tumor. Only the comparison of operative findings and the further course in a fair number of cases may prove whether or not this is true.

Following the x-ray diagnosis, biopsy is essential. The pathologist should not have to make the diagnosis from curetted threads and shreds. This is particularly stressed by Hellner[6] and also by Lichenstein.[11] The specimen submitted should consist of a good-sized piece of excised material with a small part of adjacent bone. The biopsy is the important part of the diagnosis. The likelihood of causing metastases by surgical manipulation is certainly less in a clean excision than in curettage or aspiration.

After diagnosis of the tumor has been made, the question of treatment arises and there is still no general agreement about it, as pointed out by Coley.[12]

Clean surgical excision should always be preferred. However, curettage is justified in the young. In the third decade of life or in older groups clean excision is essential because of the possibility of malignancy.

The question of x-ray treatment is controversial. In the literature there are diverse opinions as to benefits derived from x-ray therapy. A

recent paper by Coley, Higgenbottom and co-workers[13] states that roentgen treatment may bring about malignant changes in a benign giant-cell tumor. Compere[14] also warned against roentgen treatment because of the damage done by irradiation to the healthy surrounding tissue. If surgery is necessary after such therapy, the diminished vitality and viability of neighboring tissue impairs healing.

In our case reported herewith x-ray was instituted because of the metastatic nodule in the prepuce.

The therapy must be adapted to the individual case. Amputations and exarticulations may be necessary in certain cases.

Leo Mayer[15] said that this tumor is "still the problem child of the so-called benign tumors of bone."

The further course of our case will be interesting. We are optimistic about it and will report its subsequent course.

SUMMARY

A case of giant-cell tumor of the upper end of the femur has been reported, with isolated metastasis into the prepuce two and a half years after resection of the primary tumor.

REFERENCES

1. Jaffe, H., Lichtenstein, L. and Portis, R. Giant-cell tumor, its pathologic appearance, grading, supposed variants and treatment. *Arch. Path.*, 30: 993, 1940.
2. Meyerding, H. Treatment of giant-cell tumors by resection or excision and bone grafting. *J. Bone & Joint Surg.*, 27: 196, 1945.
3. Platt, H. Symposium on Sarcoma of Bone. Royal Society of Medicine. *J. Bone & Joint Surg.*, 34B: 322–323, 1952.
4. Lichenstein, L. Giant-cell tumor of bone. *J. Bone & Joint Surg.*, 33A: 143, 1951.
5. Hotz, H. W. Ueber des Riesenzellensarkom der Langen Roehrenknochen. *Virchows Arch. f. path. Anat.*, 293: 493–508, 1934.
6. Hellner, H. Die Knochengeschwulste, pp. 32–53; 150–155. Berlin, 1950. Springer-Verlag.
7. Haas, A. Observations on malignant disease of the thyroid gland. *Lancet*, 1: 1155, 1937.
8. Geschickter, C. and Copeland, M. Tumors of Bone, pp. 288–347. Philadelphia, 1949. J. B. Lippincott Co.
9. Willis, R. The Spread of Tumours in the Human Body, London, 1952. Butterworth & Co., Ltd.
10. Steward, M. and Richardson, T. Giant cell tumor of bone; 1951 Annual Meeting, Academy of Orthopedic Surgeons, Chicago, Ill. *J. Bone & Joint Surg.*, 34A: 372–386, 1952.
11. Lichtenstein, L. Bone Tumors, pp. 97–119. St. Louis, 1952. C. V. Mosby Co.
12. Coley, B. Neoplasms of Bone. New York, 1949. Paul B. Hoeber.
13. Cahan, W., Woodard, H., Higgenbottom, N., Steward, F. and Coley, B. Sarcoma arising in irradiated bone; report of 11 cases. *Cancer*, 1: 13, 1948.
14. Compere, E. Diagnosis and treatment of giant-cell tumors of bone. *J. Bone & Joint Surg.*, 35A: 822–830, 1953.
15. Mayer, L. Orthopaedic surgery in the United States of America. *J. Bone & Joint Surg.*, 32B: 461, 1950.

Bile Peritonitis

CAPT. LUTHER G. BELL, M.C., AND COMDR. HORACE D. WARDEN, M.C., *San Diego, California*

THE presence of bile in the peritoneal cavity often results in peritonitis more severe and more rapidly fatal than peritonitis resulting from other causes. This is not a new observation. The relative infrequency of the occurrence of bile peritonitis, the delay in diagnosis and the serious prognosis when treatment is delayed make it an important surgical problem. Three cases at this hospital have stimulated a review of this subject.

Etiology. McLaughlin,[1] in writing on bile peritonitis in 1942, listed a variety of ways in which this condition may be produced. The reader is referred to his work for a complete and detailed classification of the etiologic factors involved.

In the writers' experiences bile peritonitis has resulted more often from trauma and operative complications of surgery on the biliary tree. Trauma to the abdomen causing liver lacerations, bile duct injuries and rupture of the gallbladder all have resulted in bile peritonitis.[2–4] Liver laceration is the most frequent cause, bile duct injury second and rupture of the gallbladder the least likely. The gallbladder is a relatively mobile organ which is protected by the liver and is most vulnerable when it is distended.

Accessory hepatic ducts entering the gallbladder are not infrequent, and failure to recognize them at the time of cholecystectomy has resulted in leakage of bile postoperatively. Common duct obstruction not relieved at the time of surgery, with resulting increased pressure in the biliary tree, may cause bile peritonitis. Leakage may occur around a T-tube or from the cystic duct stump. Accidental removal of a T-tube before a fistulous tract has been well formed has resulted in bile peritonitis. In our opinion, such potentialities associated with gallbladder surgery necessitate draining in all cases.

Increased pressure in the biliary tract resulting from obstruction of the common duct may result in perforation of the common, the cystic or intrahepatic ducts due to weakness of some portion of these ducts or from resultant stasis, infection and ulceration. Such obstructions of the common duct are most commonly caused by calculi, but stricture, new growths and congenital cystic dilatation may also be causes.[5–8]

Medical liver biopsy has been responsible in two cases of bile peritonitis treated by the senior author but not reported here. It has been reported in a case of obstructive jaundice with increased intrahepatic biliary pressure within telangiectatic biliary ducts,[9] and also following penetration of a superficial bile duct.[10]

So-called idiopathic leakage from the biliary tract is rare but occurs often enough to be considered in a differential diagnosis of severe general peritonitis. It is theorized that the extravasation results from microscopic perforations probably resulting from infection and increased pressure in the abdomen or biliary tree. Burkitt[11] cited a case without demonstrable perforation in which he suspected obstruction of the common duct. Schlaepfer[12] reported fifteen cases in which he concluded chronic cholangitis was present almost invariably, with perforation resulting from increased intra-abdominal pressure.

Congenital abnormalities of the biliary tract in infants have resulted in bile peritonitis, the most frequent site of rupture being the common duct.[13] Byrne[14] has reported a case of a three week old child in whom bile peritonitis was caused by rupture of a congenital cyst in the region of the cystic duct.

Pathology. Clinical and experimental studies give conflicting theories and explanations as to why bile is as lethal as it often is when it is free in the peritoneal cavity. Mentzer[15] quoted others to back his opinion that sterile bile is well tolerated and of no great danger, while Norgore[3] states bile in the peritoneal cavity is dangerous and with serious sequelae.

Bile salts are known to be the toxic components of bile, the cholate radical being the important factor and there being no difference between sodium taurocholate and sodium glycocholate in toxic effect.

Miles and Jeck[16] state that in many cases of bile peritonitis the extravasation often de-

velops slowly, which may account for survival by reason of the bile being diluted with an outpouring of fluid due to peritoneal irritation, with walling off by omentum and adhesions. They believe bile in the peritoneal cavity is extremely dangerous for the following reasons: (1) It may cause congestion and edema of viscera and reticuloendothelial systems, leading to shock by fluid loss into these viscera. (2) It may inhibit the inflammatory response. (3) It may have an inwardly progressive local necrotizing effect. (4) It is virulent when associated with infection. (5) It increases the likelihood of development of purulent peritonitis and anaerobic infections of the liver, pancreas, spleen and the development of hemorrhagic pancreatitis. (6) It makes possible the absorption of toxic or lethal amounts of bile salts into the blood stream. (7) When there is survival, the sequelae are those of virulent peritonitis.

There are three main opinions as to the manner in which bile in the peritoneal cavity produces toxic symptoms: (1) that bile salts and bile acids are mainly responsible because of their toxicity;[17,18] (2) that bile is fatal only if it is infected; (3) that most of the trouble results from bile producing fluid loss from the systemic circulation into the peritoneal cavity.[19] Others have noticed a brownish fibrinous exudate covering the peritoneum of those in the late stages of bile peritonitis and believe death may result from blockage of lymphatics by this exudate.[2]

Horall[18] states that bile acids exert a toxic effect on the heart, kidneys, blood and blood capillaries, and on all tissues with which they come in contact; that bacteria have little or no effect if the peritonitis is fatal within a few hours; and that secondary surgical shock is a very important result of the toxic action of bile acids.

Symptoms. Burkitt[11] reports the one almost constant feature of this disease is an acute onset with remission of symptoms after the first attack. These patients have increasing abdominal distention, nausea, vomiting and rising pulse rate. Mild jaundice from absorption of bile in the peritoneal cavity may be evident within a few hours. Fever, colicky abdominal pain and varying degrees of shock may occur early. Bradycardia has been reported but this is not the rule.[20]

Differential diagnosis must include consideration of perforated peptic ulcer when the patient may be seen in the early acute attack. Later, peritonitis from other causes such as appendicitis with perforation, pancreatitis, intestinal obstruction and even coronary thrombosis may be suspected.

All patients who have undergone biliary tract surgery and who develop appearance of delayed surgical shock postoperatively should be suspected of having bile leakage and a resultant bile peritonitis.

Bile peritonitis developing without preceding biliary tract surgery or history of upper abdominal trauma is rarely diagnosed prior to exploratory laparotomy.

Treatment. Treatment of bile peritonitis before 1900 consisted of aspiration of the bile or bile-stained fluid, but at about that time it was noted that aspiration was not sufficient and that closure of the biliary tract wounds was also necessary. Early operation becomes imperative to prevent the shock which accompanies this disease and the resultant sequelae. Treatment should include thorough irrigation of the peritoneal cavity with dilution and removal of all free bile, repair of the site of bile leakage when possible or establishment of adequate drainage. Intravenous fluids are needed to replace the fluids lost from the systemic system into the peritoneal cavity. Dextran is probably an excellent substance to assist in combating the shock that accompanies this fluid loss. Placing abdominal drain to the operative site in biliary tract surgery is desirable, as not only may it prevent accumulation of fluid but also extensive bile drainage along such a drain may give an earlier warning that bile peritonitis is developing. Antibiotics are indicated to combat the bacterial invaders which may primarily accompany bile peritonitis or which gain a foothold in this very susceptible area secondarily.

CASE REPORTS

CASE 1. A seventy-six year old retired Naval officer had onset of severe epigastric pain one hour after eating. Pain persisted and he was hospitalized twelve hours after onset of symptoms, at which time he appeared cyanotic and was in acute abdominal distress with hyperactive bowel sounds, moderate distention, muscle guarding in the epigastrium and right upper abdomen and marked tenderness of the entire abdomen. The patient's temperature was 99.2°F., blood pressure 120/80, white blood count 12,500 and serum amylase 728 units.

On the following day his temperature rose to 102.4°F., the blood pressure was 70/56 and an ileus was present.

He was treated conservatively for acute pancreatitis. Therapy included whole blood, oxygen, antibiotics, atropine and gastric suction. However, all therapy was ineffective and he died sixty hours after onset of symptoms.

Autopsy revealed bile peritonitis with 960 cc. of bile removed from the abdominal cavity, acute cholecystitis with cholelithiasis, and acute pancreatitis. No gross perforation of the biliary or intestinal tract was found. Examination of the gallbladder showed microscopic perforations with extravasation of bile through the gallbladder wall.

CASE II. A thirty-nine year old man was admitted for treatment of a marginal jejunal ulcer following subtotal gastric resection. A higher gastric resection was done and enteroenterostomy, gastrojejunostomy and vagotomy were performed. Thirty hours after surgery, while the patient was turning to his right side in bed, severe abdominal pain suddenly developed and he went into shock with blood pressure of 80/50 and pulse of 140. Vasopressors, serum albumin and whole blood were administered, and the patient noted that abdominal pain eased after five hours. However, the abdomen remained tense and his condition was still critical. Sixteen hours after onset of these symptoms his abdomen was again opened and approximately 2,000 cc. of bile-stained fluid were found free in the peritoneal cavity. There had been no apparent leak at either of the anastomotic sites, and no other perforation was found at any point in the biliary and gastrointestinal tracts. Copious peritoneal lavage was performed with normal saline. Streptomycin and penicillin were instilled into the peritoneal cavity, and Penrose drains were placed in the left upper abdomen, beneath the liver and in the pelvis. The postoperative course was stormy; a persistent draining sinus of the left upper abdominal wall was excised and packed open to heal by granulation, and an ulcer developed in the right leg near the site of a venous cutdown which necessitated a skin graft. The patient was discharged home fifty-five days following onset of the bile peritonitis.

CASE III. A nineteen year old Navy enlisted man was admitted from the city jail where he had been placed for drunkenness. He complained of abdominal pain. His immediate condition was difficult to evaluate, but after complete studies an additional unverified and questionable history of having been beaten and kicked in the abdomen was obtained. X-ray examination revealed a fractured right second rib, and there were increasing signs and symptoms of peritonitis and shock.

Exploratory laparotomy was performed approximately sixteen hours after his injury, revealing a longitudinal laceration with maceration of the first portion of the duodenum from just distal to the pylorus to a point ¼ inch from the ampulla of Vater. There were several hundred cubic centimeters of dark, greenish fluid in the abdomen, and bile was flowing freely from the ampulla of Vater into the peritoneal cavity. A large amount of bile extended subserosally throughout the right and transverse colon, retroperitoneally, and into the right lateral abdominal wall.

Because of the precarious blood supply to the first portion of the duodenum, a sleeve resection including the pylorus was done and gastroduodenostomy performed. The postoperative course was stormy and one month later a large extraperitoneal abscess in the right flank was drained. The patient was returned to duty well three months following his injury.

COMMENTS

Bile peritonitis is a serious abdominal catastrophe with a mortality rate of 50 to 75 per cent. We believe that early diagnosis and treatment will materially reduce this figure. We would like to stress that more emphasis be placed on the disease in teaching surgical residents and interns.

We also believe that the severe shock occasionally seen in the chemical peritonitis following perforated peptic ulcer is predominately due to bile. Our clinical experience over a long period of time observing several hundred cases of perforation suggests this possibility. Two recent patients in profound shock in whom large amounts of bile-stained fluid were aspirated from the peritoneal cavity seem to emphasize this contention further. Both of these patients failed to respond to what appeared to be adequate blood but responded promptly to dextran intravenously. Although we did not use dextran in the cases reported, we recommend its use in the shock of bile peritonitis and shall do so in future cases.

In our first case the peritonitis resulted from extravasation. The same may have been true

in the second case. Even though we were unable to demonstrate any evidence whatsoever of an anastomotic leak at reoperation, such a leak would be the natural assumption. In the third case bile was flowing freely from the ampulla of Vater into the peritoneal cavity with wide subserosal extravasation of the colon and in the right side of the abdomen.

Severe shock is a prominent feature in this condition and should arouse suspicion as the possible cause in any case of peritonitis. In two of our cases shock was severe. Of McLaughlin's[1] eight patients, profound shock was suffered by five, all of whom died. Shock comes on early if bile is disseminated throughout the peritoneal cavity. Shock is less severe and less often seen if the collection is localized. It appears that shock may be in direct proportion to the amount of bile present and its general dissemination.

We not only urge early treatment of the disease but also thorough peritoneal lavage at laparotomy. It seems logical to assume that lavage with normal saline is more effective than toilet with suction alone. Any bile not removed by suction will be diluted and the loss of plasma-like fluid into the peritoneal cavity will be lessened.

In the conclusion of this discussion it might be well to differentiate between biliary peritonitis and biliary ascites. Ravdin et al.[21] have shown that biliary peritonitis requires the presence of free bile salts in the peritoneal cavity, the source of which is a leak in the biliary tree. In biliary ascites, which is attendant upon hepatic and portal obstruction, the bile salts present come from the blood stream by diapedesis rather than from extravasation or perforation of the biliary tree.

Biliary peritonitis usually is associated with or complicated by infection, while biliary ascites is not associated with infection unless it is introduced from without or extends from an infected abdominal organ.

SUMMARY

The subject of bile peritonitis has been reviewed and three cases summarized. Attention is called to the seriousness of this clinical entity. It is our impression that the severe shock associated with perforated duodenal and jejunal ulcers usually can be attributed to the presence of bile in the peritoneal cavity. Early diagnosis and surgery are imperative. We wish to stress thorough peritoneal irrigation at the time of surgery, with repair and drainage of the site of bile leakage. We would suggest the use of dextran in the treatment of shock associated with bile peritonitis.

REFERENCES

1. McLaughlin, C. W., Jr. Bile peritonitis. *Ann. Surg.*, 115: 240–248, 1942.
2. Newell, C. E. Traumatic rupture of gallbladder and liver: report of base with generalized bile peritonitis. *Am. J. Surg.*, 76: 466–471, 1948.
3. Norgore, M. Traumatic rupture of the gallbladder: case reports and notes on choleperitoneum. *Ann. Surg.*, 123: 127–134, 1946.
4. Hickey, N. F. and Stevenson, V. L. Traumatic rupture of the choledochus associated with an acute hemorrhagic pancreatitis and a bile peritonitis. *Ann. Surg.*, 128: 1178–1183, 1948.
5. Gariepy, L. J., Capano, O. A. and Gardner, L. W. Nontraumatic rupture of the common bile duct. *Am. J. Surg.*, 81: 357–362, 1951.
6. Fournier, D. J. Bile peritonitis due to spontaneous rupture of a dilated intrahepatic duct. *California Med.*, 72: 245–246, 1950.
7. Dreiling, D. A. Spontaneous rupture of the common bile duct following choledocholithotomy. *S. Clin. North America*, 27: 381–387, 1947.
8. Hart, D. E. Spontaneous perforation of the common bile duct. *Ann. Surg.*, 133: 280–282, 1951.
9. Rubenstone, A. I., Mintz, S. S. and Meranze, D. R. A case of fatal bile peritonitis following liver needle biopsy. *Ann. Int. Med.*, 36: 166–168, 1952.
10. Gallison, D. T., Jr. and Skinner, D. Bile peritonitis complicating needle biopsy of liver. *New England J. Med.*, 243: 47–50, 1950.
11. Burkitt, D. P. Biliary peritonitis without demonstrable perforation. *Brit. M. J.*, 2: 155–157, 1946.
12. Schlaepfer, K. The etiology of bile peritonitis. *J. Internat. Coll. Surgeons*, 2: 427–433, 1939.
13. Caulfield, E. Bile peritonitis in infancy. *Am. J. Dis. Child.*, 52: 1348–1360, 1936.
14. Byrne, J. J. and Bottomley, G. T. Bile peritonitis in infancy. *Am. J. Dis. Child.*, 85: 694–697, 1953.
15. Mentzer, S. H. Bile peritonitis. *Arch. Surg.*, 29: 227–241, 1934.
16. Miles, R. M. and Jeck, H. S. Observations on experimental bile peritonitis. *Surgery*, 34: 445–456, 1953.
17. Manson, M. H. and Eginton, C. T. The cause of death in bile peritonitis. *Surgery*, 4: 392–404, 1938.
18. Horall, O. H. Bile: Its Toxicity and Relation to Disease, pp. 210–224. Chicago, 1938. Univ. Chicago Press.
19. Harkins, H. N., Harmon, P. H. and Hudson, J. E. Lethal factors in bile peritonitis. *Arch. Surg.*, 33: 576–609, 1936.
20. Storck, A. N. Diagnosis in abdominal trauma. *Am. J. Surg.*, 61: 21–42, 1942.
21. Ravdin, I. S., Morrison, M. E. and Smyth, C. M., Jr. Bile peritonitis and bile ascites. *Ann. Surg.*, 89: 867–877, 1929.

Alterations in Blood Coagulation Mechanism after Incompatible Blood Transfusion

CLINICAL AND EXPERIMENTAL OBSERVATIONS

CAPT. DONALD G. MCKAY, M.C., LT. COL. ROBERT M. HARDAWAY, III, M.C., LIEUT. G. H. WAHLE, JR., M.C., CPL. RICHARD EDELSTEIN AND PVT. DONALD E. TARTOCK,
Fort Belvoir, Virginia

From the Departments of Pathology and Surgery, 7071st ASU, U. S. Army Hospital, Fort Belvoir, Virginia. Aided by a grant from The Office of the Surgeon General, United States Army, Project 6-60-01-002.

HEMORRHAGE of a minor or even major size has been frequently noted following incompatible blood transfusion. Wiener[1] called attention to the fact that frequently a hemorrhagic tendency develops immediately after the transfusion, and blood may ooze from the site of transfusion, from the gums, uterus (in postpartum cases) or any fresh puncture made in the skin for the purpose of treatment. In 1922 Astrowe[2] reported a case of an eighteen month old child who entered the hospital with bilateral otitis media which was treated by incision and drainage of much pus. The following week mastoiditis appeared and the child was transfused with 180 cc. of her mother's citrated blood without reaction. Twenty days later a similar transfusion of 130 cc. was given. This resulted in vomiting, cyanosis and unconsciousness, with labored respirations and shock. Hemoglobin appeared in the urine and bleeding occurred from the incision into the mastoid process and from the lips. The child became anuric immediately but eventually recovered. Subsequently it was determined that the child was Group O and the mother Group A.

Levine and Segall[3] reported a case of a repeat transfusion of 500 ml. of blood which was followed by chills, fever, cyanosis, dyspnea, weak pulse, pain in the lumbar region and vomiting of blood-stained mucus. Blood also oozed from the gums. Hematemesis and hemorrhage from the rectum and vagina took place seven hours later. Blood was found in the urine. After five days these symptoms stopped abruptly and the patient recovered.

In 1935 Parr and Krischner[4] reported a case of hemorrhage and death following a transfusion of what was apparently compatible blood according to their technic at the time. The patient had five children and a history of three abortions in the early months of pregnancy. For the forty days preceding admission she had been bleeding from an attempted induced abortion and was severely anemic. The uterus was the size of a three months' pregnancy and the vagina contained blood clots. A direct transfusion of 200 ml. of her husband's blood produced vertigo, nausea and bright flush of the skin. Labored breathing and cyanosis soon developed. An hour and a half after the transfusion, bleeding occurred from the needle holes of the hypodermic injections and the transfusion site. She vomited blood-stained mucus and blood oozed from the vagina. The urine became bloody and four and a half hours after the transfusion the patient died.

Abramson[5] reported a similar case in the same year. His patient was a twenty-four year old gravida II, para I, who was a few days from term and had a hemoglobin of 34 per cent. The patient was Group O and her husband was Group A. One hundred milliliters of the husband's citrated blood were injected when the patient complained of a heavy feeling in the chest, dyspnea, nausea, diarrhea and vomited blood-stained mucus. After stopping the transfusion it was again started and after an additional 75 ml. cyanosis, dyspnea, weak pulse, cough and hematemesis developed. Four and a half hours later she bled from the vagina, gums and roof of the mouth, and from a small stab wound of the ear which had been made the day before to obtain a blood sample. One-half

hour later she was delivered of a stillborn infant and bled profusely from the vagina. Hemorrhage with incoagulable blood continued until her death one hour later.

In 1949 Seldon[6] pointed out that patients under anesthesia develop a marked tendency toward bleeding at the operative site as one of the cardinal signs of an incompatible blood transfusion.

In 1951 Friesen and Nelson[7] reported seven cases of massive hemorrhage associated with blood transfusion. These cases are of considerable interest, inasmuch as they were all undergoing operations and the first evidence of a reaction was a hemorrhagic state consisting mainly of oozing from the cut surfaces of the incision. Only two of these patients survived the bleeding episode. In only one patient was it demonstrated that the donor blood was incompatible. The cause of the massive hemorrhage in this group of patients could not be demonstrated. Three had thrombocytopenia, but no abnormalities of bleeding, clotting or prothrombin times were detected in most instances. Administration of toluidine blue, vitamin K, vitamin C, protamine, calcium gluconate, antihemophilic globulin and thrombin (intravenously as well as topical administration) were ineffective in controlling the bleeding. These authors[7] concluded that the reduction in circulating platelets played a role in the bleeding dyscrasia, but that the nature of the clotting defect remained unknown.

Muirhead[8] encountered a hemorrhagic state in 24.3 per cent of a total of thirty-seven incompatible transfusion reactions. Eight of the patients in this series survived, but one died directly as the result of hemorrhages. The hemorrhagic state appeared to be associated with the infusion of large volumes of incompatible blood, such as 380 ml. in one case, 500 ml. in five cases, and 1 L. in three cases. The clinical course of this group demonstrated the troublesome nature of the hemorrhagic state. Three patients received the incompatible blood for postpartum hemorrhage and continued to bleed from the uterus. One was controlled by uterine packing after a period of shock. One not only bled from the uterus but also developed subcutaneous ecchymoses and had a prolonged interval of shock. The third postpartum patient eventually succumbed to the bleeding. One patient received 1 L. of incompatible blood and oozed from the uterus for eight days, during which time 15 pints of blood were given. Uterine curettage, hot saline irrigation of the uterine cavity and uterine packing were unsuccessful in coping with the hemorrhage. Hysterectomy was performed but the patient died the following day and at autopsy a large hematoma was found in the pelvis although all major vessels appeared to be adequately tied. A hemorrhagic state developed in five surgical patients. The rapid development of the tendency to bleed was demonstrated by the profuse oozing of blood either during or shortly after the transfusion. One patient remained in shock after hysterectomy for fibroids; the abdomen was reopened and a hematoma was found in the pelvis. Another patient who had had thoracoplasty continued to ooze profusely from the wound for twenty-four hours and had to be returned to the operating room in order to pack the wound more securely. One man bled for two days following a colostomy. The fourth patient bled copiously during and after spinal fusion. Hypotension was marked for seven hours, during which time 4 L. of compatible blood were administered. An additional copious hemorrhage occurred eighteen hours postoperatively and death followed rapidly. The ninth patient bled actively from the gums only. Muirhead believed that the cause of the hemorrhage was unknown. However, he noted that in four patients there was an increase in circulating heparin-like substance. Toluidine blue was given to these patients in doses of 100 to 200 mg. in 500 ml. of 5 per cent dextrose in thirty to sixty minutes. One patient exhibited a transient decrease in the uterine bleeding but bled subsequently. Another, who had almost stopped bleeding, ceased bleeding altogether when the dye was administered. Two patients who were bleeding profusely stopped bleeding during the infusion of 200 mg. of toluidine blue and the Allen-titration test reverted to normal.

In 1954 Hardaway, McKay and Williams[9] reported four cases of hemorrhage following incompatible blood transfusion. All of their patients had prolonged prothrombin times. Two exhibited fibrinolytic activity. Case 4 was a twenty-eight year old white multipara who had a normal and uneventful delivery, with minimal blood loss. Because of a hemoglobin of 7.3 gm. a transfusion was started thirty-six hours after delivery. The patient was Group O, Rh positive, and the donor blood was Group A,

Rh positive. Following 300 ml. of blood she had a chill and vomited blood. Hemoglobin appeared in the urine and she began to bleed from the gums and uterus. Venous blood samples revealed that her blood was incoagulable (failure to clot in two days) and that this was due to afibrinogenemia. Other changes in the coagulation system consisted of a prolonged bleeding time, thrombocytopenia, hypoprothrombinemia and a marked fibrinolytic activity. Administration of 8.4 gm. of fibrinogen caused abrupt cessation of the bleeding and restored the coagulation time to almost normal limits in a matter of hours. At least in the early stage of this reaction there was no evidence of anticoagulant activity.

Postmortem studies have also indicated the hemorrhagic nature of some transfusion reactions. In 1932 Lattes[10] described small hemorrhages or emboli in the brain, mesentery, endocardium and gastrointestinal tract at autopsy. Lindau[11] described ulceration and hemorrhage in the colon. In other organs, pinpoint hemorrhages in serous membranes, in kidneys and liver have been found.

Experimental studies of incompatible transfusion reactions have shed some light on the problems. In 1875 Landois[12] described hyaline thrombi in the mesentery of dogs subjected to incompatible transfusion reactions.

Melnick et al.[13] observed that in two of their animals the clinical picture of anaphylactic shock developed. Intense salivation, vomiting, labored respiration, involuntary urination and defecation, and a low blood pressure were noted. "The blood coagulability was so markedly reduced that hemorrhages from the sites of puncture in the femoral artery and jugular vein could only be controlled with great difficulty; tremendous hematomas were obtained in the thighs." One dog exhibited a prolongation of the clotting time from two minutes to more than six hours.

Young et al.[14] in similar experiments noted that there was a transient decrease in the blood platelets and leukocytes, an increase in the coagulation time and a decrease in the prothrombin concentration in some of the animals undergoing an incompatible transfusion reaction.

Nelson et al.[15] produced a hemorrhagic state in dogs by infusing hemolyzed blood. The coagulation time was prolonged and there was poor clot retraction. The hypocoagulable blood could be made to clot *in vitro* by addition of thromboplastin or fresh blood from another dog. This reversal was only temporary *in vivo*. Hemorrhage occurred from the entire gut which was contracted, pitted, granular and studded with petechiae. Bloody effusion occurred into the serous cavities and there were petechiae in the lungs, serosal surfaces and along blood vessels. Microscopically the liver and spleen showed parenchymal congestion with erythrocytes and pigment.

The experiments described in this report were performed in an attempt to correlate these scattered observations in one experimental series with a view toward determining the role of fibrinogenopenia in the coagulation defect. In addition, since cortisone has been shown to modify the blood coagulation mechanism, the influence of this hormone on incompatible transfusion reaction was also studied.

MATERIALS AND METHODS

Thirteen experiments* were performed on one female and eight male mongrel dogs. The animals were anesthetized by use of intravenous sodium pentobarbital with a dose which was sufficient for a period of six to eight hours of anesthesia. The amount varied between 5 and 7 ml. of a solution containing 60 mg./ml. An incompatible blood transfusion of 50 to 300 ml. of outdated human bank blood or sheep blood was then given into the external jugular vein. One group of animals was given 100 mg. of cortisone a day for three days preceding the transfusion. The other group had either no preparation or were dehydrated for three days prior to transfusion. Coagulation times were performed according to a modification of the Lee-White method.[16] Platelet counts were done by the direct method using the Rees-Ecker diluting fluid.[17] Prothrombin times were done by a one-stage method using simplastin® as the thromboplastic agent. Fibrinogen content was determined by the method of Seegers:[18] 1 ml. of plasma was diluted with 29 ml. of physiologic saline, 1 ml. phosphate buffer at pH 6.4, 0.5 ml. of 1 per cent $CaCl_2$, and 100 NIH units of thrombin were added to clot the fibrinogen. A micro-Kjeldahl analysis was then performed on the fibrin clot after removing

* We wish to express appreciation to Major Howard C. Poulin and Lieut. James L. Fowler of the Veterinary Corps for their cooperation.

it with a glass rod and dissolving it in 4 ml. of 0.25 N NaOH. Fibrinogenolysis was determined by the method of Crosby[19]: plasma was incubated at 37°C. for two hours and a fibrinogen content determined. Fibrinogenolytic activity was considered to be the amount of fibrinogen lost in two hours. The presence of fibrinolysis was tested by observing whole clotted blood in the incubator at 37°C. for forty-eight hours. Clot retraction was not measured quantitatively but was judged as good or poor on the basis of gross observation of clots. White blood counts were done in the routine manner described by Ham.[17] Antithrombin titrations were performed by a modification of the technic by Ratnoff,[16] i.e., by measuring the clotting times of varying dilutions of thrombin in 0.1 ml. of saline added to 0.2 ml. of plasma. Whole blood anticoagulant was detected according to a slight modification of the method described by Frohmeyer.[17]

These tests were run on samples of blood drawn from the external jugular veins before administration of cortisone, just prior to the incompatible transfusion, at one-hour intervals for three hours following the transfusion, and at seven hours after the start of the experiment.

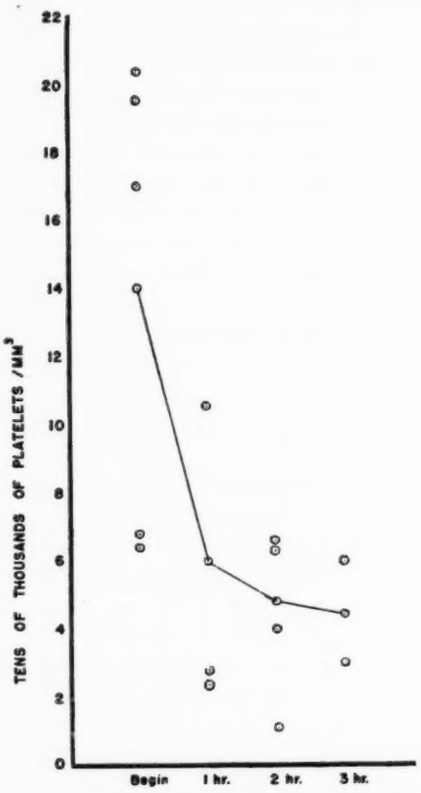


FIG. 1. Decrease in dogs' circulating blood platelets following transfusion of human blood.

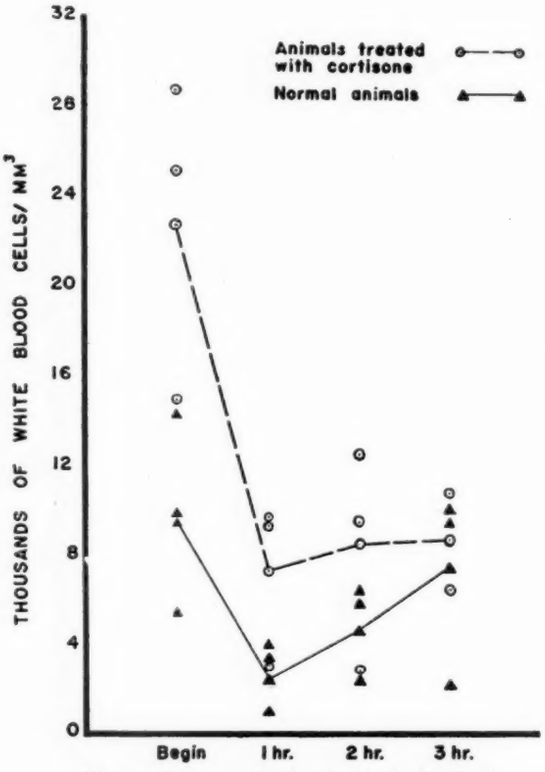


FIG. 2. Decrease in dogs' circulating leukocytes following transfusion of human blood.

OBSERVATIONS

Hemorrhage. Clinical hemorrhage occurred in all but two of the experiments. The amount, character and location of the hemorrhages were quite variable from one animal to the next. The most constant finding was gross blood in the stools. This varied from a streaking of blood to a massive, almost exsanguinating hemorrhage from the rectum and occurred either during the transfusion or within several hours following the reaction. Two dogs vomited blood-streaked mucus. Two developed large hematomas at the site of needle punctures and two developed a generalized oozing from the margins of an abdominal incision.

Platelets. (*Fig.* 1.) The average platelet count was 140,000 per mm.³ The count dropped precipitously to less than half the initial count in the first hour following the incompatible transfusion. It remained at this low level for

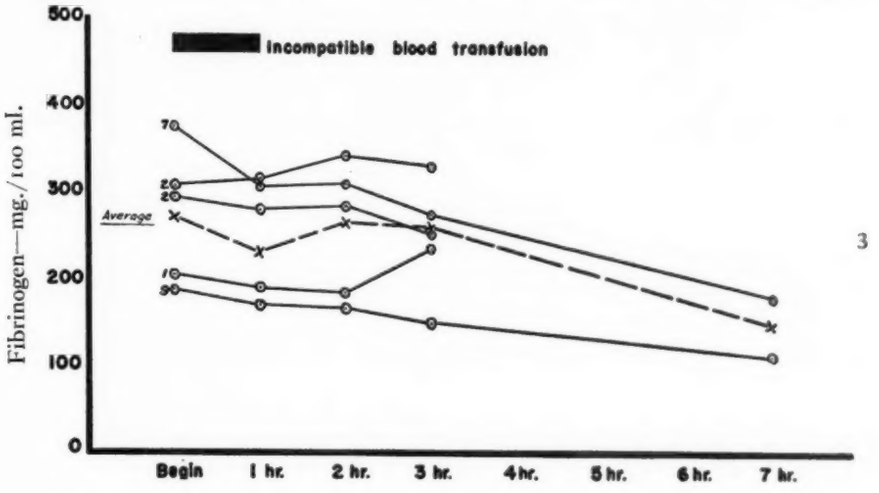
the next three hours but tended to rise slightly at the end of seven hours.

Clot Retraction. The initial sample in each experiment exhibited good clot retraction while all subsequent specimens through the seventh hour showed poor retraction.

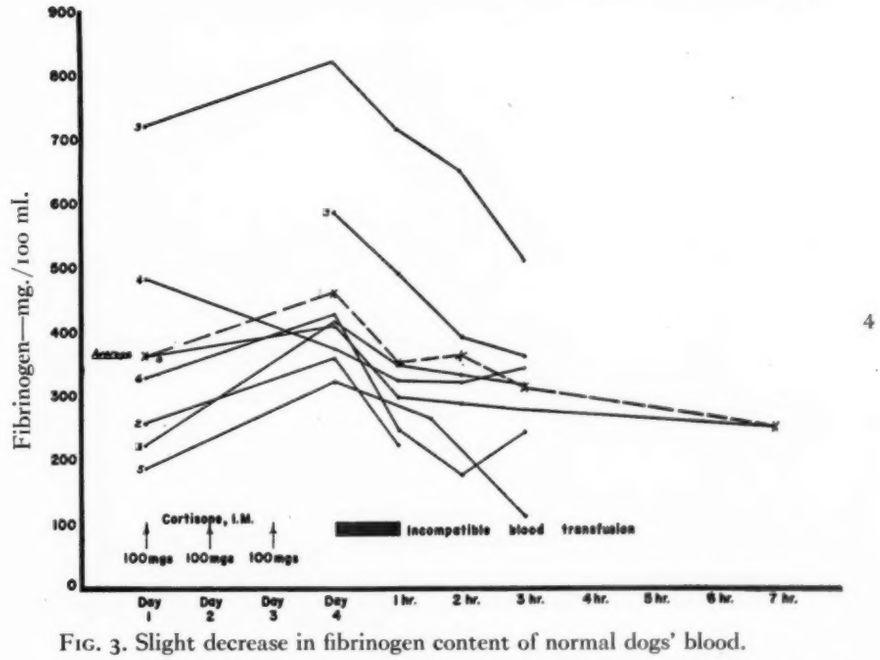
White Blood Cells. (*Fig.* 2.) The average normal white blood count was 9,140 per mm.^{3}, which dropped as rapidly as the platelet count in the first hour following transfusion to a level of 2,760 per mm.^{3} In the next two hours the white count rose again to 7,300 per mm.^{3} Cortisone treatment raised the white count to 22,900 per mm.^{3} The decrease in white cells following the incompatible transfusion was quantitatively greater but proportionately the same in cortisone treated dogs as in normal dogs.

Fibrinogen. (*Figs.* 3 *and* 4.) The average fibrinogen level of the normal dog was 269 mg. per 100 ml. with a high of 483 and a low of 185. Following transfusion the fibrinogen fell an average of 40 mg. in the first hour and over a seven-hour period dropped gradually to a level of 150 mg. per 100 ml.

Treatment with cortisone caused an eleva-



3



4

FIG. 3. Slight decrease in fibrinogen content of normal dogs' blood.

FIG. 4. Blood fibrinogen levels of dogs pre-treated with cortisone followed by incompatible blood transfusion.

tion of the fibrinogen. The average rise in the three-day period was 100 mg. The one animal whose fibrinogen content dropped during cortisone treatment was the only female in this group.

The fibrinogen content following transfusion

Prothrombin Time. (*Fig.* 6.) The average one-stage prothrombin time of the normal dogs was 9.5 seconds, while that of the cortisone-treated dogs was 6.7 seconds. In both groups the prothrombin time was gradually prolonged during the seven-hour period. The prolongation

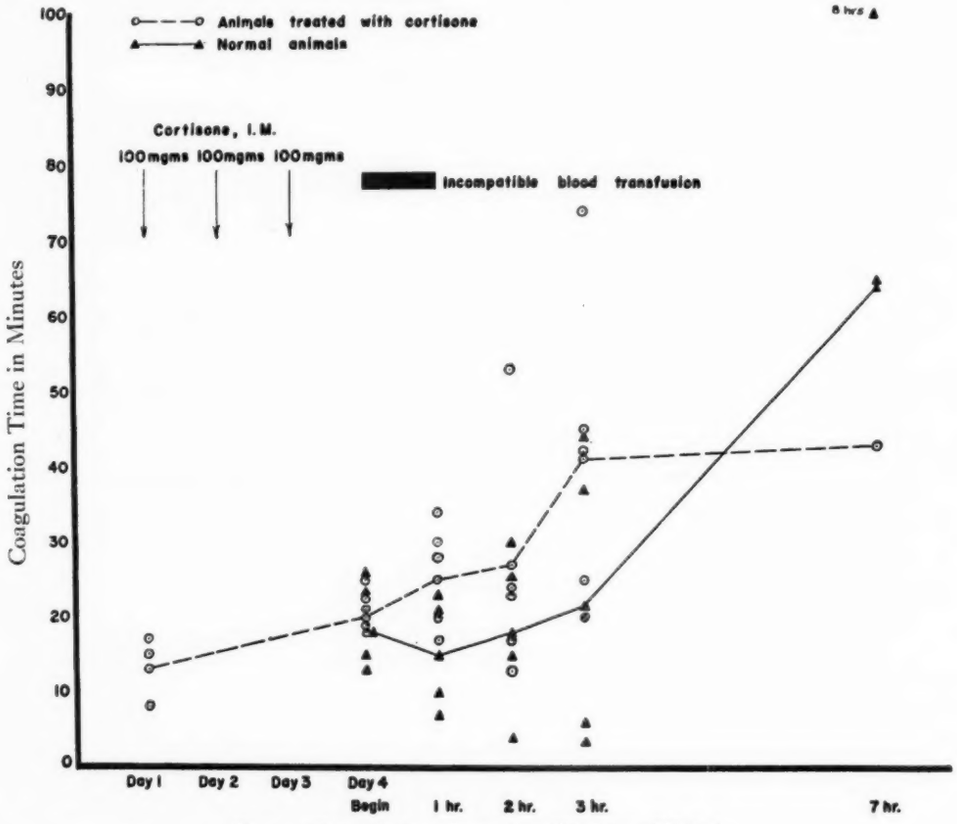


FIG. 5. Coagulation times (modified Lee-White).

reaction in cortisone treated animals fell more precipitously in the first hour than it did in the normal dogs. The average drop was 112 mg. In the subsequent six hours the decline in fibrinogen occurred at the same slow rate as in the normal dogs.

Coagulation Time (*Fig.* 5.) The average coagulation time of the normal dogs was thirteen minutes. A slight prolongation to twenty minutes took place during the three days of cortisone administration. Following the incompatible transfusion reaction the coagulation time varied a great deal. In some animals the coagulation time was shortened. In the majority it was markedly prolonged. The average figures indicate a gradual prolongation of the clotting time during the seven-hour period of observation. The blood of one animal failed to clot for a period of eight hours.

was slight but definite, and at the end of the experiment averaged fourteen seconds.

Whole Blood Anticoagulant. (*Fig.* 7.) As did the coagulation time, the anticoagulant activity showed considerable variation following the transfusion. Prior to the experiment there was little or no evidence of an anticoagulant. In general, anticoagulant activity appeared in slight amount at the end of one hour and was most prominent at the end of three hours. By the end of the seventh hour it appeared to have declined toward normal.

Antithrombin Activity. (*Fig.* 8.) Antithrombin titrations were performed in five experiments. A marked increase in the antithrombin titer occurred in each case, following the transfusion. However, the rate at which the antithrombin titer rose and fell was extremely variable. In two experiments the antithrombin

titer rose progressively in the three hours following transfusion and appeared to be increasing at the end of seven hours. In two experiments the titer rose and reached a peak at the end of two hours and then fell to normal within the seven-hour period during which the observations were made. Cases illustrative of these variations are presented. (Fig. 8.) In the fifth case the titer rose during the first hour, declined during the second hour and rose again at the end of three hours.

Toluidine Blue. The *in vitro* use of small amounts of toluidine blue in the coagulation tubes shortened the coagulation time in two cases. In one case the clotting time was elevated to forty-four minutes at the end of one hour while the addition of toluidine blue maintained the clotting time at a normal level. In the second experiment toluidine blue shortened the clotting time from eight hours to fifty minutes.

Fibrinolysin and Fibrinogenolysis. In none of these experiments was there clear-cut evidence of lysis of clotted whole blood within a forty-eight-hour period. Similarly, the fibrinogen content of the plasma was not altered after two hours incubation at 37°C., and therefore no fibrinogenolytic activity was demonstrated.

COMMENTS

Interpretation of Hematologic Changes in the Dog. The mechanism that best explains the changes in the coagulation factors in these experiments is that suggested by Crosby[19] for the "plasma transfusion reaction" in patients with paroxysmal noctural hemoglobinuria; that is, a tendency toward intravascular coagulation. Such a tendency could account for most of the observed alterations. If intravascular coagulation were to take place, one would expect a utilization of the clotting factors with a reduction of fibrinogen and prothrombin, and the subsequent development of hypocoagulable blood. These were among the observed changes in these experiments. The actual precipitating factor that initiates the reaction is possibly agglutination and partial destruction of blood platelets. The fact that the platelets drop precipitously in the first few hours and then rise slowly toward normal, as does the white blood count, suggests that these cellular elements are temporarily sequestrated somewhere in the vascular system, perhaps agglutinated and some destroyed. With destruction of a few platelets and release of "platelet enzyme," thromboplastin would be formed and the tendency to coagulation established.

The factor or factors responsible for agglutination and destruction of platelets remains unknown. Heterologous plasma, the stroma of hemolyzed red cells or the agglutinated masses

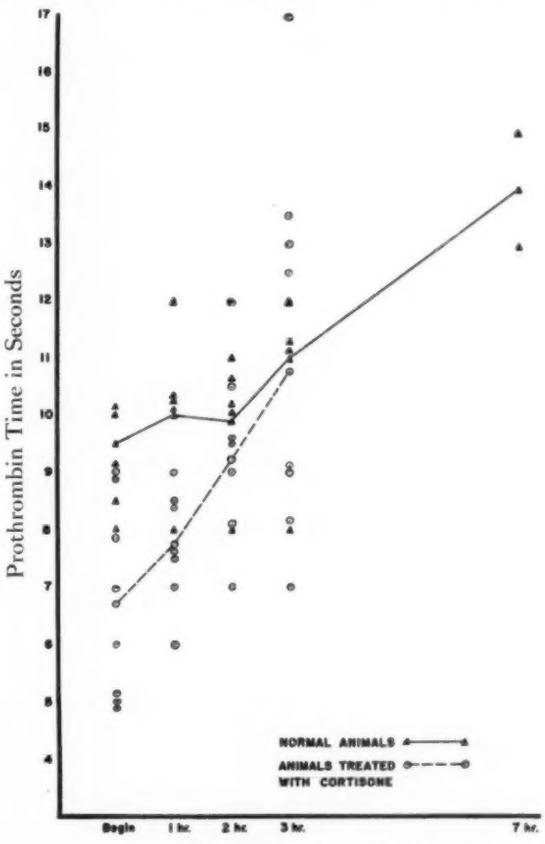


FIG. 6. Plasma prothrombin times.

of erythrocytic impinging on the capillary endothelium might be responsible. That it is not hemoglobin is suggested by the work of Nelson et al.[15] They stated that plasma hemoglobin alone was apparently not the sole cause of the hemorrhages, since intravenous administration of distilled water sufficient to raise the plasma hemoglobin above 1.0 gm. per cent did not cause the condition.

That this reaction is entirely non-specific has been pointed out by Crosby[19] who noted that a variety of materials injected into the blood streams are capable of eliciting a similar response in the coagulation system. Such agents as plasma (normal) in patients with paroxysmal nocturnal hemoglobinuria, Wittes' peptone, anaphylactic shock, typhoid bacilli and a wide variety of Shwartzman active materials are among them.

The appearance of an anticoagulant following the episode of intravascular coagulation may represent a defense of the body against this clotting tendency. Ratnoff[20] noted the development of an anticoagulant in dogs injected intravenously with thromboplastin.

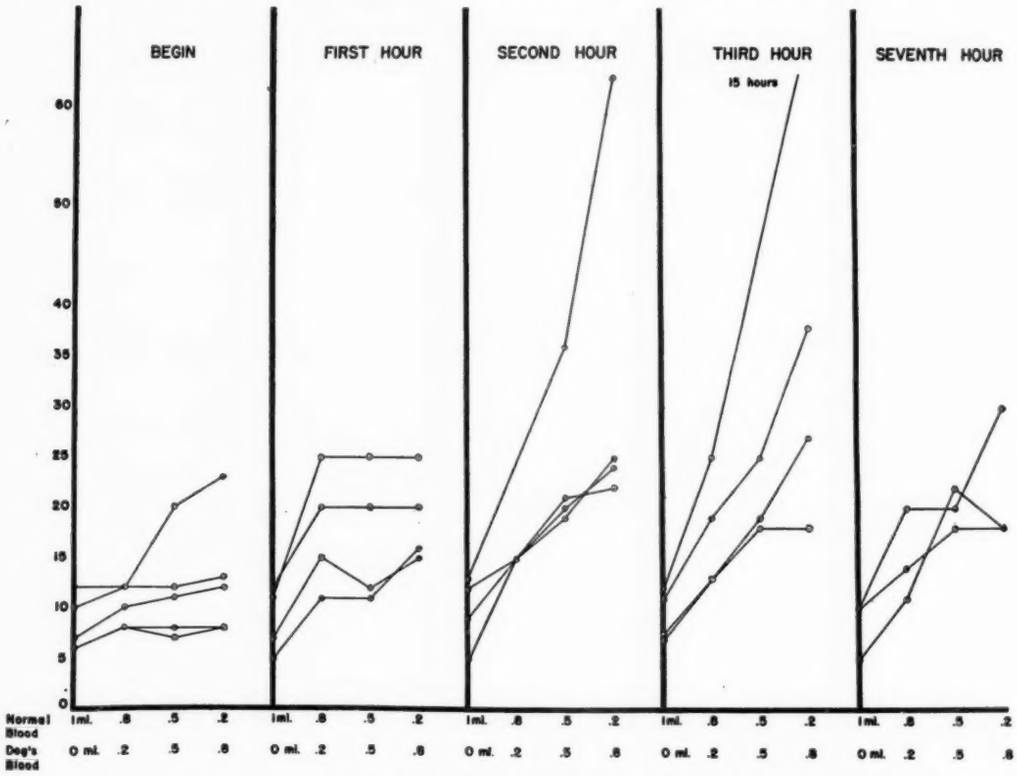


FIG. 7. The prolonging effect of dogs' blood on the coagulation time of normal blood.

The anticoagulant is antithrombic and is partially counteracted by toluidine blue. It therefore appears to have properties resembling those of heparin. The clinical hemorrhage in these experiments appeared to be related more directly to the periods of greatest anticoagulant activity than to any of the other changes in the blood.

The Influence of Pre-treatment with Cortisone. Cortisone injection for three days preceding the transfusion reaction caused an elevation of the blood fibrinogen in all but one animal. This was associated with a marked elevation of the blood sedimentation rate. Many factors appear to be responsible for the regulation of the blood fibrinogen level, and steroid hormones are among them. It is of interest to note that Tagnon[21] produced an increase in blood fibrinogen with estrogen administration and a decrease with androgen treatment in a patient with prostatic carcinoma. He attributed these alterations in fibrinogen to concomitant changes in the fibrinolytic activity of the blood. This same mechanism may be in operation in the normal dog with cortisone treatment, but we were unable to detect any alteration of fibrinolytic activity by the methods used.

Cortisone pre-treatment caused an elevation of the white blood count and was apparently responsible for a slight prolongation of the coagulation time. At the same time it caused a greater and more rapid decrease in the fibrinogen concentration in the first hour following incompatible blood transfusion. It seems to have been responsible for an increase in the tendency to coagulation in this reaction.

Comparison of Clinical and Experimental Observations. There are many similarities between the hematologic changes noted in human cases and those of the animal experiments. They share in common thrombocytopenia, decrease in fibrinogen concentration, prolongation of the coagulation time, prolongation of the prothrombin time and the appearance of a circulating anticoagulant with some of the properties of heparin.

Nevertheless, there are two outstanding differences. The first is the presence of a marked

fibrinolytic activity in the human cases, and its absence in the animal experiments reported herein. The second is that in the one case in man in which fibrinogen was determined, a complete afibrinogenemia existed; whereas in the dog experiments, the fibrinogen decreased

the main blood clotting factors should be obtained, and, depending on the results, (1) purified fibrinogen and/or (2) antiheparin agents (toluidine blue or possibly protamine sulfate) should be administered. In certain cases these might be life-saving procedures.

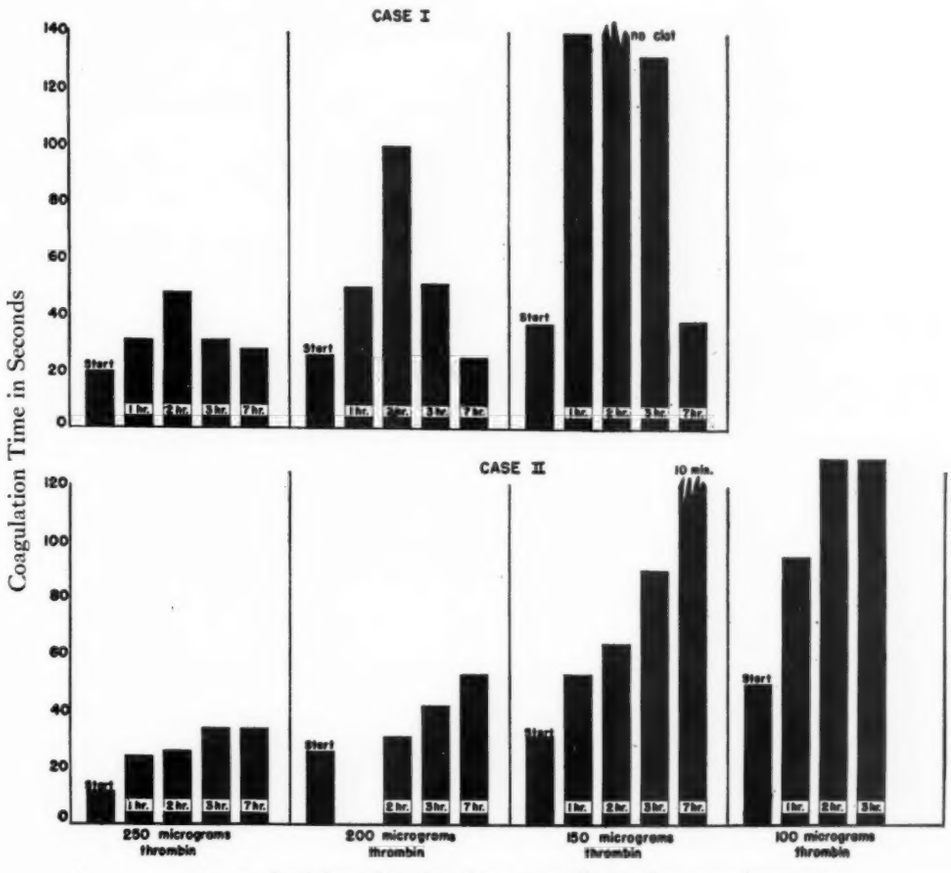


FIG. 8. Antithrombin titrations; two illustrative experiments.

but never disappeared completely. These may represent species differences in the response to incompatible blood, or they may mean that certain preparatory conditions existed in the human cases that have not been achieved in the animal experiments.

Management of Hemorrhage with Incompatible Transfusion Reaction. Aside from the theoretic consideration, there are two practical implications of the knowledge thus far obtained. The hemorrhagic state in man appears to be due to two basic causes (1) afibrinogenemia or fibrinogenopenia and (2) the development of a heparinoid anticoagulant. From the standpoint of clinical management in any such case, an immediate estimate of all

SUMMARY

1. The hemorrhagic diathasis following an incompatible blood transfusion reaction is associated with thrombocytopenia, prolongation of the coagulation time, prolongation of the prothrombin time, a decrease in the circulating white blood cells, the appearance of fibrinolytic activity and of a "heparinoid" anticoagulant.

(2) The reaction is somewhat different in dogs inasmuch as the fibrinogen level does not decrease as markedly as in the human case, nor does fibrinolytic activity appear.

3. It is suggested that the management of these cases be a complete immediate estimate

of all the major blood clotting factors with a subsequent replacement of fibrinogen or the use of an antiheparin agent wherever indicated.

Acknowledgment: We wish to express our thanks to Corporals John K. Witherspoon, Marvin Numeroff and Charles Applegate for their help in conducting these experiments.

REFERENCES

1. Wiener, A. S. Blood Groups and Transfusion. Springfield, Ill., 1943. Charles C Thomas.
2. Astrowe, P. S. Hemolysis following transfusion. *J. A. M. A.*, 79: 1511–1514, 1922.
3. Levine, E. C. and Segall, H. N. Post transfusion reaction. Alterations in blood after ether anesthesia and after blood transfusion. *Surg., Gynec. & Obst.*, 35: 313–319, 1922.
4. Parr, L. W. and Krischner, H. Hemolytic transfusion fatality with donor and recipient in the same blood group. *J. A. M. A.*, 98: 47, 1932.
5. Abramson, M. Hemolytic transfusion reaction with death. *Journal Lancet*, 55: 805–807, 1935.
6. Seldon, T. H. Transfusion reaction among patients under general anesthesia. *Mississippi Valley M. J.*, 71: 124–126, 1949.
7. Friesen, S. R. and Nelson, R. M. The occurrence of massive generalized wound bleeding during operation, with reference to the possible role of blood transfusions in its etiology. *Am. Surgeon*, 17: 609–622, 1951.
8. Muirhead, E. E. Incompatible blood transfusion with emphasis on acute renal failure. *Surg., Gynec. & Obst.*, 92: 734–746, 1951.
9. Hardaway, R. M., McKay, D. G. and Williams, J. H. Lower nephron nephrosis (ischemuric nephrosis) with special reference to hemorrhagic diathesis following incompatible blood transfusion reaction. *Am. J. Surg.*, 87: 41–49, 1954.
10. Lattes, L. In: Whitby, L. E. H. and Britton, C. J. C. Disorders of the Blood. p. 535, Philadelphia, 1946. The Blakiston Co.
11. Lindau. Cited by Wiener.[1]
12. Landois. Die Transfusion des Blutes. Leipzig, 1875.
13. Melnick, D., Burack, E. and Cowgill, G. R. Development of incompatibilities in dogs by repeated infusions of red blood cells. *Proc. Soc. Exper. Biol. & Med.*, 33: 616–621, 1935.
14. Young, L. E., Erwin, D. M. and Yuile, C. L. Hemolytic reactions produced in dogs by transfusion of incompatible dog blood and plasma. *Blood*, 4: 1218, 1949.
15. Nelson, R. M., Eder, W. P., Eddy, F. D., Karlson, K. E. and Dennis, C. Production of a hemorrhagic state by the infusion of hemolyzed blood. *Proc. Soc. Exper. Biol. & Med.*, 73: 208–209, 1950.
16. Ratnoff, O. D. and Vosburg, G. J. Observations on the clotting defect in amniotic fluid embolism. *New England J. Med.*, 247: 970–973, 1952.
17. Ham, T. H. A Syllabus of Laboratory Examination in Clinical Diagnosis. Cambridge, Mass., 1952. Harvard University Press.
18. Seegers, W. H. Blood Coagulation. In: The Enzymes, vol. 1. Edited by Sumner, J. B. and Myrbäck, K. New York, 1951. Academic Press.
19. Crosby, W. H. and Stefanini, M. Pathogenesis of the plasma transfusion reaction with especial reference to the blood coagulation system. *J. Lab. & Clin. Med.*, 40: 374–386, 1952; and personal communication.
20. Ratnoff, O. D. and Conley, C. L. Studies on afibrinogenemia. II. The defibrinating effect on dog blood of intravenous injection of thromboplastic material. *Bull. Johns Hopkins Hosp.*, 88: 414–424, 1951.
21. Tagnon, H. J., Schulman, P., Whitmore, W. F. and Leone, L. A. Prostatic fibrinolysin. Study of a case illustrating the role in hemorrhagic diathesis of cancer of the prostate. *Am. J. Med.*, 15: 875–884, 1953.

Cardiac Arrest

PRITCHARD T. C. LAM, M.D., *Honolulu, Hawaii*, JOHN T. WRZESINSKI, M.D., *Lincoln, Nebraska*, AND BENEDICT R. WALSKE, M.D., *Lincoln, Nebraska*

From the Veterans Administration Hospital, Lincoln, Nebraska.

THE sudden failure of the heart during inhalation anesthesia resulting in death was first recorded in 1848. The knowledge of resuscitation of acute cardiac arrest from 1848 to 1945 accumulated slowly and was gleaned from a small number of isolated case reports and experimental work on animals. There is much information available from animal experimentation in this field; however, the species differences in behavior results in information not always applicable to the human subject.

Case reports of cardiac resuscitation are increasing in modern day surgical publications and evaluation of collected series of many hundreds of cases is permitting a more rational approach. Two additional cases are added to the literature to aid in evaluation of this complex and confusing subject. In a recent publication, Leeds[1] requested that a complete and careful record of clinical observations of all cases be published for statistics regarding the effectiveness of treatment. Hurwitt[2] noted that no previous cases of cardiac rupture caused by massage have been reported. Case 1 of this report is presented as a second case of cardiac rupture for the statistical record.

Cardiac arrest is ordinarily considered an infrequent occurrence; yet, it perhaps occurs quite frequently only to initiate its own normal rhythm spontaneously. Many factors may play a part in the sudden failure of the heart to maintain the circulation. Any one or all of these factors may contribute in precipitating the arrest, especially in the presence of ischemic areas in the myocardium, the result of coronary arteriosclerosis. Excessive secretion of adrenalin brought about by hypoglycemia, emotional states, surgical manipulation of the adrenal glands, or the hypersecretion of adrenergic tumors increases irritability of the myocardium. Cardiac arrest may result when the potassium concentration of the blood reaches abnormally high or low levels. Oxygen deficiency increases vagal tone and also increases the secretion of adrenalin, thus further sensitizing the myocardium. It also depresses the respiratory center. The anoxia of anemia produces an increase of the vagus tone centrally and reinforces the action of accompanying hypercapnia upon the cardio-inhibitory center. Hypercapnia with its consequent reduction of pH of the blood results in a direct stimulation of the vagus center, increasing its reflex irritability, and consequently the excitability of the vagus nerve. It also leads to depression of the excitability of the peripheral accelerator cardiac nerves. Hemorrhage, as well as hypoxia, produces an increased sensitivity of the carotid sinus reflex. Action of bacteria, toxins, pyrogens and transfusion reactions can all contribute to the precipitation of arrest. Anesthetic agents, such as chloroform, cyclopropane or ethyl chloride have the ability to sensitize the heart to the action of epinephrine. Intravenous barbiturates and cyclopropane also have a parasympathomimetic effect upon the heart. Sensitivity to the various drugs used in spinal anesthesia and intravenous therapy may cause sudden cardiac arrest. Excessively deep general anesthesia causes respiratory depression and subsequent cardiac arrest.

TREATMENT

Much has been written regarding the treatment of cardiac arrest but very little concerning prophylaxis, as noted by Dinsmore[3] in a recent article. Preoperatively, much thought should be given to the very young and the very old patients. Cardiac arrest seems to occur more commonly in these two groups. In the young, hypoxia apparently sensitizes the myocardium to a more active vagovagal reflex. In the older individual, arteriosclerosis and coronary artery disease contributes to myocardial ischemia, thus sensitizing the heart by an oxygen lack.

Hypoxia and/or hypercapnia as a common denominator, coupled with myocardial sensitization and triggered by a vagovagal reflex, appear to be the primary causes of cardiac arrest. A concentrated effort must be made to control these factors. Preoperative blood volume should be returned to normal, anemia should be treated and electrolyte balance established. Routine large preoperative doses of barbiturate followed by large doses of narcotics are to be condemned for the central and peripheral respiratory depression they produce. Induction must be smooth with the properly chosen anesthetic. Serious consideration should be given before using cyclopropane in cardiac patients and especially in those demonstrating arrhythmias. The same consideration must be given highly emotional individuals in whom high circulating levels of adrenalin may be present. Adrenalin administered to an individual anesthetized with cyclopropane may give rise to ventricular fibrillation. Routine use of curare and curare-like drugs with sodium pentothal® apparently sets up an ideal situation for cardiac arrest. The use of the endotracheal tube has brought an advantage to surgery that is unrivaled by any other single advance except perhaps the antibiotics; however, it must be realized that insertion or adjustment of the endotracheal tube at the wrong moment may bring about disastrous results by virtue of inciting the vagovagal reflex.

Adequate oxygenation, particularly during operative procedures lasting over an hour, cannot be overemphasized. Preoperative preparation of selected patients with a high concentration of oxygen for fifteen or twenty minutes may be indicated in an attempt to relieve a possible oxygen debt. Special care not to stimulate or otherwise disturb the patient during the excitement stage of anesthesia is reemphasized. Tracheobronchial secretions which accumulate during the operative procedure tend to lead to anoxia. These secretions are easily available and easily handled when the endotracheal tube is in place.

In children it is notoriously easy to reach the respiratory arrest level of anesthesia. Dr. Potts in a series of 500 operations for congenital heart disease, as quoted by Dinsmore,[3] states that he has had no cases of cardiac arrests since using a light plane of anesthesia; the child at no time releases its grip on the fingers of the anesthetist. Apparently, it is safer to keep the level of anesthesia light.

In adults carelessly administered and improperly followed spinal anesthesia has more than once set up a chain of events leading to cardiac arrest. The level of anesthesia must be checked and rechecked as it has been known to advance upward even after the normal period which it ordinarily takes to "set."

When all other precautions are taken, the job of diminishing the vagovagal reflex is relegated to atropine sulfate. In the present day of formidable and lengthy procedures it has been forgotten somehow that the influence of atropine is apparently exerted for about ninety minutes in an effective concentration. Reid[4] has found that an ordinary dose of atropine sulfate has the maximum effect in about fifteen to twenty minutes, has added action for forty-five minutes and has sufficient protection for approximately ninety minutes. In order to protect fully the anesthetized individual against vagovagal reflexes, it is emphasized that the atropine dose must be repeated from ninety to 120 minutes during and immediately following the operative procedure.

An arrhythmia occurring in a previously regular heart is a warning that the heart is being subjected to unusual stress. It has long since been noted that intravenous procaine hydrochloride has a pronounced beneficial effect on the arrhythmic heart and serious consideration must be given to its use as an adjunct in therapy in such an instance. Additionally, the vagus fibers may be blocked by procaine infiltration if indicated either at the celiac ganglion during abdominal surgery or at the aortic arch during thoracotomy. Attention should be paid to the concentration of carbon dioxide in the circulating blood during surgery. The soda lime within the closed circuit of the anesthesia machine must be functioning properly. In short, prophylaxis involves the prevention of myocardial sensitization and of vagovagal reflexes.

Should an arrest or ventricular fibrillation occur, immediate thoracotomy and massage of the heart is indicated. If abdominal surgery is in progress, an opening may be made in the diaphragm and massage instituted by that route. There is little question, however, that the thoracic route is the most efficacious and should be used whenever possible. Transdiaphragmatic massage of the heart without

opening the diaphragm is considered ineffective. If cardiac arrest is in question, an absence of pulse followed by cessation of voluntary respiration is a signal for immediate cardiac massage. It is far better to massage a weakly beating heart than to delay massage should arrest have occurred. The patient should be placed in slight Trendelenburg position and immediate positive pressure respiration established. This should be done briefly without an endotracheal tube if one is not in place to prevent further delay; but as soon as practicable the endotrachal tube should be inserted. Mouth-to-mouth respiration may be the only type of positive pressure artificial respiration available and must be resorted to if the gas machine is not present. The chest is most effectively opened in the fourth left interspace anteriorly, severing costal cartilages near the sternum for additional exposure. There should be no delay in preparing an aseptic field. Such delay could be the difference between survival and death of the patient. A scalpel and retractor are the only essential instruments.

In the beginning, time is not wasted in opening the pericardium although after a minute or two of successful massage such may be accomplished to facilitate the procedure. Massage is performed by placing the right thumb over the anterior surface of the heart and the fingers posteriorly. Rhythmic massage at 40–50 beats per minute appears to be adequate in most instances; however, rhythmic massage up to 120 per minute may double the cardiac output.[5] The only disadvantage of the more rapid rate is early fatigue of the operator. It may be said then that as rapid a rate as possible up to 120 per minute consistent with the endurance of the operator and his assistants is ideal. Positive pressure respiration is established simultaneously with massage. In arrest 1:1000 epinephrine in 0.5 to 1 cc. quantities either with or without 10 cc. of 1 per cent procaine solution should be injected into the right ventricular cavity as soon as a short period of massage and artificial respiration has been performed. Every few minutes the heart must be re-evaluated for resumption of spontaneous rhythm and massage re-instituted as needed. The circulation must be concurrently supported with positive pressure intravenous or intraarterial blood transfusions or other fluids if blood is not available. The blood volume must be increased and the cardiac filling maintained. It must be remembered that elastic bandaging of the extremities diverts more blood to the viscera. In addition, an assistant may be utilized to compress or cross-clamp the thoracic aorta in an effort to direct the much-needed blood to the central nervous system. Atropine sulfate must be given in dosage of at least $\frac{1}{150}$ gr. to the average adult either into the ventricular cavity or intravenously. Stevenson, Reed and Hinton[6] in a recent report point out a case in which massage was carried on for two hours without response but succeeded immediately upon injection of 3 cc. of 2 per cent barium chloride into the left ventricle.

When the heart is under direct vision and fibrillary movements are observed, cardiac massage must still be employed before attempting defibrillation. After effective massage is established, 10 cc. of 1 per cent procaine injected into the cavity of the right heart and 5 per cent procaine applied directly to the surface of the fibrillating muscle should be administered as has been recommended by Beck.[7] The object in treatment is to convert the fibrillation into a standstill after which the latter is treated as indicated. If defibrillation fails by this method, a 110 volt, 60 cycle alternating current of 1 to 1.5 amperes for .1 to .5 seconds is passed through the heart. Saline-moistened, gauze-covered electrodes are placed on the anterior and posterior surface of the heart. The heart muscle is shocked to a standstill. More than one shock may be necessary to bring about standstill or normal rhythm, whichever occurs first. When standstill occurs, it is treated by massage as a primary case. Recently commercial defibrillators have become available. More recently a cardiac pacemaker has become commercially available. When the electrodes of this unit are applied to the heart in the region of the sino-auricular node, normal ventricular contractions may be carried on indefinitely and manual massage can thus be eliminated.

CASE REPORTS

Case 1. H. J. H. (No. 46,173), a fifty-five year old white man, was admitted to the Chest Service on May 19, 1952. Bronchoscopy revealed a neoplasm obstructing the right upper lobe bronchus. Biopsy demonstrated a grade 1 squamous cell carcinoma of the bronchus. A right pneumonectomy under cyclopropane

anesthesia was performed on May 21st. The bronchus was amputated at its junction, with the trachea. The patient tolerated the procedure well and was in good condition upon transfer to the ward. Late in the afternoon, there was a gradual drop in blood pressure and the pulse became imperceptible. After rapid administration of blood and vasopressor drugs, the blood pressure returned to 66 mm. of mercury. The blood pressure had returned to 120 mm. of mercury by the time the operating room was prepared. The blood pressure again dropped to zero and pulse became imperceptible upon turning the patient to the lateral position. The right thoracic cavity was opened rapidly through the previous thoracotomy wound and found to be completely filled with clotted and fluid blood. The blood was removed rapidly from the right thoracic cavity and inspection revealed a large rent in the pulmonary artery where a No. 1 silk ligature had cut through the vessel. At this time the heart was still beating feebly although irregularly. The rent in the right pulmonary artery was closed rapidly with a continuous arterial suture. At this time the heart had come to a standstill. The pericardium was opened and massage instituted. Blood was given under positive pressure both intravenously and directly into the right atrium. An attempt also was made to infuse blood under pressure into the femoral artery; however, technical difficulties permitted only a few hundred cc. by this route. Cardiac filling was considered inadequate throughout most of the procedure and only a few spontaneous beats would follow cessation of massage. Rupture of the right ventricular musculature occurred after approximately sixty minutes of massage. This was rapidly closed with interrupted silk sutures and massage continued. After another fifteen minutes of massage, rupture of the musculature again occurred in another area and was treated as the first. After ninety minutes of massage there was no evidence of cardiac filling and the myocardium no longer had the ability to respond to stimulation. At this point the case was considered hopeless and massage was discontinued. Epinephrine, 1 cc. of 1:1000, and 10 cc. of 1 per cent procaine had been injected several times throughout the ninety minutes of massage.

At autopsy the heart was found to be of average size and shape and weighed 325 gm. Two rents were seen in the right ventricle which were closed with interrupted black silk sutures. Considerable extravasation of blood was present in the epicardium. Internal examination of the heart revealed the endocardium smooth and glistening. Leaflets and cusps were thin and pliable. Chordae tendineae were thin and papillary muscles were of average size. The myocardium showed some ecchymotic areas, especially over the apices of both ventricles. Coronary vessels showed only a minimal amount of arteriosclerosis.

Microscopically, sections were taken through the ventricles, interventricular septum and auriculoventricular septum. There was evidence of extensive maceration of muscle bundles and extravasation of blood into the interstitium. The muscle bundles were fractured and undergoing early degenerative changes, loss of striation and atrophy of the nuclei. There were rather extensive hemorrhages throughout the epicardial fat as well as the subendocardial tissue. Sections taken through the auriculoventricular septum revealed only a minimal amount of myocardial hemorrhage.

Case II. L. L. B. (No. 49,086), a thirty-two year old white man, was admitted to the hospital on August 11, 1953, for an emergency appendectomy. Examination of the heart and lungs revealed no abnormalities. Abdominal examination revealed tenderness in the right lower quadrant, moderate right rectus spasm and questionable evidence of a mass in the right lower quadrant. Complete blood count on admission showed 12,800 white blood cells, 77 per cent neutrophils, 23 per cent lymphocytes, 3,300,000 red blood cells and 10 gm. hemoglobin. The bleeding time was two minutes and coagulation time three minutes. Urinalysis revealed no abnormality other than an occasional white blood cell per high-power field. A scout film of the abdomen failed to show any evidence of renal calculi or any other pathologic disorder. A preoperative diagnosis of acute appendicitis or possibly regional enteritis was considered. The patient experienced increasing pain in the right lower abdominal quadrant and asked for operative intervention.

The patient was taken to the operating room six hours after admission to the hospital. The abdomen was explored through a lower right rectus incision. Exploration revealed an annular constricting lesion of the ascending colon

about 3 inches above the ileocecal junction. Considerable edema of the peritoneal and retroperitoneal tissues in the vicinity of the tumor was also noted. The lesion was considered to be a carcinoma of the ascending colon. Right hemicolectomy was performed without incident. Blood in the amount of 1,500 cc. was transfused during the operative procedure.

Near the end of the operation an attempt was made to pass a nasogastric tube. A short period of difficulty in respiration and cyanosis followed. It was thought that the tube passed down the trachea rather than the esophagus. Aspiration of the pharynx followed by subsequent passage of the tube gave rise to no further respiratory difficulty. The patient was returned to his room in good general condition.

About a half hour after returning to his room the nurse in charge reported cyanosis which was followed by cessation of respiration. The resident surgeon, who happened to be in his office next door, was immediately called and artificial respiration was started. This effort forced a moderate amount of secretions into the pharynx which was then aspirated. At this time absence of pulse was reported whereupon the cardiac arrest cart was requested. The left chest was opened through the fourth interspace anteriorly sectioning the fourth and fifth cartilages near the sternum. The pericardium was opened and massage instituted. Simultaneously, the anesthetist inserted an endotracheal tube and started artificial respiration by rhythmic bag pressure. Massage was continued for about fifty minutes but spontaneous rhythm did not occur until 1 cc. of 1:1000 epinephrine was injected into the right ventricle. The heart was observed for several minutes and the chest then rapidly closed. It was estimated that five to seven minutes passed between cardiac arrest and cardiac massage.

Blood pressure and pulse almost immediately returned to normal figures. Later the same evening an electrocardiographic tracing revealed evidence of right bundle branch block and sinus tachycardia. The heart beat spontaneously for seventeen hours but spontaneous respiration did not return. Artificial respiration was continued by rhythmic bag pressure and by the iron lung. The patient did not return to consciousness and expired at 12:32 P.M. on August 12th.

At autopsy the lung, for the most part, was airless and had the gross appearance of pulmonary edema. This was confirmed on microscopic section. The heart apparently stopped in systole. It was firm in consistency and weighed 250 gm. The epicardium was smooth and glistening. In the region of the posterior descending branch of the coronary vessels there were several small ecchymotic areas in the subepicardium. Upon opening the heart the endocardium was found to be smooth and glistening. The valve rings and cusps showed nothing of importance. The coronary vessels showed no abnormalities. The ascending aorta appeared normal. Microscopic sections of the heart revealed normal cardiac muscle. No cellular infiltrates, necrosis or evidence of myocardial degeneration was seen. The brain was found to be markedly softened to the point of liquefaction necrosis. The total weight of the brain was 1,500 gm. The cortex showed atrophy and the entire brain was in a semiliquid state. Microscopically, the brain showed marked degenerative and early necrotic changes consisting of neurolysis, microglia and glial cell infiltration and edema throughout.

COMMENTS

Case 1 represents a middle-aged patient that was subjected to an uneventful pneumonectomy. In retrospect it becomes evident that the ligature partially cut through the pulmonary artery. It can be assumed that bleeding was at first slow in that rapid transfusion restored blood pressure from an unobtainable level to 120 mm. of mercury. It can be assumed also that at the time of positioning of the patient the rent in the pulmonary artery became markedly widened and he thereby bled rapidly into the right hemithorax. It is estimated that the time interval from loss of palpable pulse to beginning of massage was less than three minutes; however, blood replacement was rather ineffective as noted by the poor cardiac filling. Efforts to replace circulating volume by positive pressure methods as described was not rapid enough to permit effective massage within the critical period.

The technic of massage varied little from methods described and recommended by others. The thumb was placed anteriorly and the four fingers posteriorly. The heart was held full within the palm of the hand. The move-

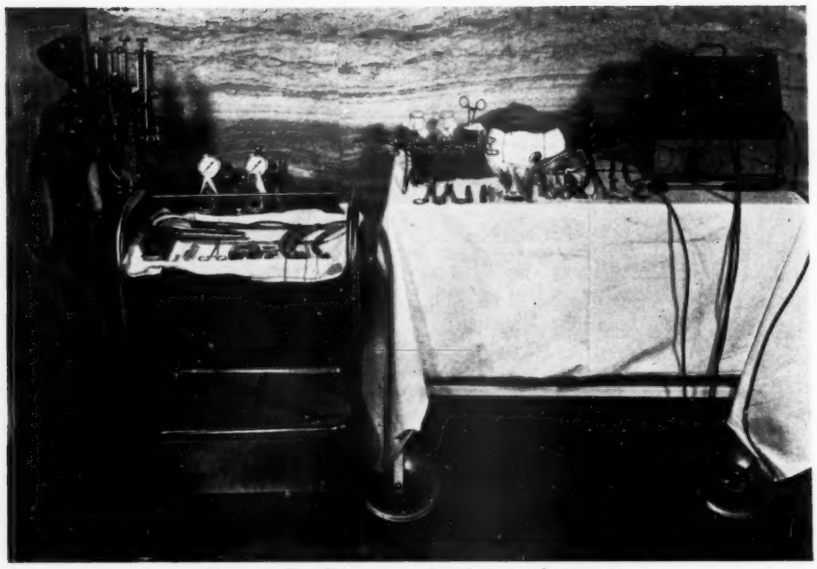


FIG. 1. Cardiac resuscitation equipment.

ments were firmly accomplished yet without undue force. The rate of massage was estimated to average between 40 and 50 per minute. In view of the fact that rupture of the right ventricle occurred after sixty minutes of massage is evidence enough that this is indeed a traumatic procedure. The maneuver perhaps becomes more traumatic in the presence of an undistended ventricle and the concomitant flaccid musculature. The use of an automatic pacemaker would eliminate such trauma and, although not absolutely essential, should, if possible, be added to the list of equipment on the cardiac resuscitation cart. Figure 1 represents the equipment held readily available for cardiac resuscitation at this hospital.

The primary cause for cardiac arrest in Case 1 is quite apparent: rapid loss of circulating blood volume producing a state of relative anemia, cardiac sensitization and associated secondary reflexes resulting in subsequent arrest. Failure to respond to resuscitative measures apparently was based on the inability to restore adequate circulating volume within the critical period.

Case 11 in contrast represents a relatively young patient who also succumbed to cardiac arrest. In view of acute appendicitis being considered the most likely diagnosis, the anesthetist did not intubate the trachea as is routine for more protracted operative procedures. For this reason, secretions were not periodically aspirated from the trachea and bronchi. It is quite likely that the short period of cyanosis near the end of the operative procedure and again after return to his room was directly related to secretions which had accumulated in the respiratory passages. Blood replacement of 1,500 cc. was in excess of the amount lost throughout the operative procedure; however, a moderately severe anemia existed prior to the operative procedure. Hypoxia, hypercapnia and anemia triggered by aspiration of the pharynx in the absence of adequate blocking effect of atropine appears to be sufficient cause for cardiac arrest in this case. Since the occurrence of this catastrophe, the administration of the usual preoperative dose of atropine is repeated every two hours as a routine throughout prolonged operative procedures. It is believed that although it is only one part of a chain of events, it is an important prophylactic measure.

Although spontaneous rhythm was not established early in this case, an injection of 1 cc. of 1:1000 epinephrine into the right ventricle promptly restored normal circulation. The gradual deterioration of the patient's general condition and his inability to establish spontaneous respiration was evidence of failure to restore circulation within the critical period. This was further confirmed by the condition of the brain at autopsy. In spite of the presence of a surgeon, anesthetist and resuscitative equipment all within 100 feet of the patient on the same floor, the critical period of three to five minutes was exceeded. It is not likely that many patients outside the operating room

will be resuscitated from a state of cardiac arrest; however, it should not deter us in our efforts.

SUMMARY

1. Two cases of cardiac arrest are presented and the problems encountered are discussed.

2. The various prophylactic measures are emphasized. Prophylaxis is the best means of meeting the over-all problem of cardiac arrest and if practiced conscientiously will unquestionably reduce the incidence to a minimum. The repeated doses of atropine to block as far as possible the trigger mechanism of a vagovagal reflex in an already sensitized heart is believed a worth while addition to the prophylactic regimen.

3. The various resuscitative measures are outlined.

4. Cardiac massage is a traumatic procedure as is noted by rupture of the right ventricle in Case I and a lesser degree of damage in Case II.

5. A means of positive pressure oxygen, a knife and retractor are the only essential pieces of resuscitative equipment; however, a defibrillator and automatic pacemaker are worth while investments.

6. The urgency of immediate massage is again emphasized.

REFERENCES

1. Leeds, S. E. Cardiac resuscitation. *J. A. M. A.*, 152: 1409, 1953.
2. Hurwitt, E. S. and Seidenberg, B. Rupture of the heart during cardiac massage. *Ann. Surg.*, 137: 115–119, 1953.
3. Dinsmore, R. S. Trends of surgery in the last decade. *Ann. Surg.*, 138: 289, 1953.
4. Reid, L. C., Stephenson, H. E., Jr. and Hinton, J. W. Cardiac arrest. *Arch. Surg.*, 64: 319, 1952.
5. Johnson, J. and Kirby, C. K. Cardiac resuscitation. *S. Clin. North America*, 29: 1748, 1949.
6. Reid, L. C., Stephenson, H. E., Jr. and Hinton, J. W. Some common denominators in 1,200 cases of cardiac arrest. *Ann. Surg.*, 137: 731, 1953.
7. Surgical Practice of the Lahey Clinic. Philadelphia, 1951. W. B. Saunders Co.

Evaluation of Lumbar Sympathectomy in Advanced Arteriosclerotic Peripheral Vascular Disease Complicated by Gangrene

LESTER L. OSTROVE, M.D., *New York, New York*

From the Surgical Service of Lincoln and Lebanon Hospitals, New York, New York.

THERE is considerable interest in the therapy of arteriosclerotic peripheral vascular disease with lumbar sympathectomy. This is demonstrated by the sizeable literature dealing with this subject during the past fifteen years. As a result of this accumulated experience it has been shown that lumbar sympathectomy is of considerable value in the care of early arteriosclerotic peripheral vascular disease. However, the role of this operation in the advanced disease complicated by gangrene is not well established and requires further elucidation. This situation seems unusual in that intermittent claudication, which must be considered as a sign of advanced peripheral arteriosclerosis, seems to respond satisfactorily.[1–3,5,8,11–13,16–18]

The purpose of this paper is to attempt to clarify the effect of lumbar sympathectomy in advanced arteriosclerotic peripheral vascular disease complicated by gangrene of a complete toe, toes or forefoot. In order to add significance to the findings a group of patients with similar physical signs and symptoms, but in whom lumbar sympathectomy was not utilized, are used as controls.

Telford and Simmons[17] state that cases with gangrene complicated by infection will deteriorate with greater rapidity following lumbar sympathectomy. Atlas[1] believes that sympathectomy is contraindicated in those advanced cases characterized by pallor on elevation, dependent engorgement and dry inelastic skin with atrophy of the underlying muscles. Smith, Gullickser and Campbell[16] reported that the advantage of this operation in the more advanced cases of arteriosclerosis has not been demonstrated. Freeman[7] emphasized the so-called paradoxic effect of lumbar sympathectomy. The theory, as elaborated, discusses the role of the arteriovenous shunts in diverting vital blood flow from the deeper tissues to the more superficial. This action in the far advanced arteriosclerotic is said to accelerate the gangrenous process. Hermann stated unequivocally, in discussing Freeman's paper, that lumbar sympathectomy should not be performed in the patient with extensive structural changes of the peripheral arteries unassociated with increased vasomotor tone. Edwards and Crane[6] believe that sympathectomy cannot be of much value in the presence of deep necrosis or gangrene. Kirschner,[12] in a critical review dealing with essentially the same type of material as is presented in this paper, concurred with the latter viewpoint. He mentions, however, that he could not find any direct causal relationship between progression of tissue necrosis and lumbar sympathectomy. Lee et al.[13] state in their paper that all cases with deep gangrene will require higher amputation despite lumbar sympathectomy.

On the other hand, one cannot fail to be impressed with the group of independent investigators who have noted worth while effects from lumbar sympathectomies in obliterative arteriosclerotic peripheral vascular disease complicated by gangrene. In independent papers Coller[3] and Gerber[9] found that 73 and 70 per cent, respectively, of their patients did not require a major amputation after lumbar sympathectomy. In a small series Jemerin[10] was enthusiastic about the value of this operation. Blaine and Campbell[2] considered lumbar sympathectomy an effective tool in limiting the spread of gangrene. Telford and Simmons[17] express the opinion that lumbar sympathectomy makes it possible to perform a much less radical amputation. Smith, Gullickser and Campbell[16] stated that those patients upon whom a lumbar sympathectomy had been

performed showed a lower morbidity and higher incidence of primary wound healing after a major amputation. DeBakey et al.,[5] stated that following sympathectomy a less radical operation is needed and there is a possible arrest of the gangrenous process. Frymark and Sullivan[8] believe that in the peripheral arteriosclerotic patient with gangrene one should try lumbar sympathectomy and minimal amputation first, providing the patient's general condition warrants them.

This wide variation in opinions may of course be due to the small number of cases making up most series. It is also possible that in some of these the gangrenous areas may have been superficial patches of tissue rather than deep necrosis.

MATERIAL

This report is based upon an analysis of cases observed in a large municipal hospital and from the ward services of a voluntary hospital. The cases included for study have all met the following criteria: the presence of obliterative arteriosclerotic peripheral vascular disease as manifested by absent, palpable pedal pulses and the presence of gangrene of a complete toe or toes and often a portion of the forefoot. In approximately 95 per cent of the cases the disease was complicated by some degree of infection in the affected toe or toes. In addition, most of this group had one or more of the following symptoms: cold feet, rest pain and intermittent claudication. Sixty-nine per cent of these patients had their disease process complicated by diabetes mellitus.

This series, as previously mentioned, is divided into two parts: a smaller one of thirty-three patients in whom lumbar sympathectomy was performed, and a larger group consisting of seventy-nine patients in whom the operation was not performed. In all other respects both categories were treated similarly. All of the patients were observed in the period from 1948 through 1953. In all of the cases in which lumbar sympathectomy was reported there was confirmation of the ganglion tract by the Department of Pathology. The operation was accomplished by the muscle-splitting retroperitoneal technic and usually the second and third ganglia were removed. This procedure as used herein was often utilized as a last resort. It was performed shortly after admission in some cases, and after many weeks in others. Again in some the local pathologic condition was all but ignored; in others it was dealt with vigorously either before, during or after operation. The only contraindications to the procedure that were considered were rapidly spreading gangrene of the foot and the presence of a complicating severe systemic illness. The results are summarized in Table 1.

COMMENTS

It is noted that the mortality rate in both groups appears to be unusually high. However, it is believed that in dealing with patients in this physical condition one can anticipate a relatively high mortality as compared to those individuals with evidence of arteriosclerosis of a lesser degree. An additional factor that must be reckoned with in the great majority of these people is the presence of nutritional disturbances, chronic low blood volume and complicating disease which tend to increase the hazards of their care. Despite the fact that many of these deaths, such as coronary occlusions, cerebrovascular accidents and renal insufficiency, were not directly related to the local pathologic condition, they are included in the results as failures. Although this may color the evaluation of the operation, it is believed that in this group they cannot be excluded. Lumbar sympathectomy *per se* was considered the predominant factor in only one fatality. This was a patient with far advanced kidney disease who succumbed to renal insufficiency postoperatively. This patient should not have been selected for the operation.

The causes of death in those having lumbar sympathectomy are as follows: one cerebrovascular accident, one coronary occlusion, one uremia; two patients refused amputation for gangrene of foot and died of toxemia; in two cases gangrene of the other foot developed and the patient died of toxemia.

The results as presented herein would tend to substantiate the opinion that lumbar sympathectomy, as it is currently employed, does not beneficially influence the course of far advanced peripheral vascular arteriosclerosis complicated by gangrene. It will be seen that 53 per cent of those not having sympathectomy required an amputation through the leg or thigh. In those patients in whom lumbar sympathectomy was utilized 47.5 per cent required a major limb amputation. This difference is not considered significant. Statistically

this small series cannot prove or disprove the impression concerning the value of this operation in influencing the site of amputation. Nevertheless, it was this observer's impression that at the time of amputation in those that had lumbar sympathectomy, the circulation clinical result can be obtained in 60 per cent of the cases. In the remaining 40 per cent it is suggested that a ganglionectomy excising T12 and L1 in addition might accomplish the desired effect. Lowenberg and Morton[14] have shown in anatomic studies the interconnection of the

TABLE 1

PATIENTS WITH ADVANCED ARTERIOSCLEROTIC PERIPHERAL VASCULAR DISEASE MANIFESTED BY GANGRENE

Site of Amputation	Treated with Lumbar Sympathectomy (33)			Not Treated with Lumbar Sympathectomy (79)		
	Major Limb Amputation 18*			Major Limb Amputation 46*		
	No. Performed	Failures	Deaths†	No. Performed	Failures	Deaths†
Transmetatarsal	2	1	..	8	7	1
Leg	12	6	4	16	4	2
Supracondylar	6	1	1	30	8	8
	Summary: 16 patients required higher amputation (47.5%)			*Summary:* 42 patients required higher amputation (53%)		
	* Excludes transmetatarsal			* Excludes transmetatarsal		
	† Seven deaths. Remaining 2 died without major amputation			† Fourteen deaths. Remaining 2 died without major amputation		

in general appeared to be much greater than those that did not. It is significant that other observers concur with this finding. The value of a knee joint and leg stump in rehabilitation is well established. The worth of any procedure that will assist in accomplishing this end is self-evident. Concerning transmetatarsal amputation in this far advanced group, the only conclusion that can be drawn is that it is extremely difficult to select the patients upon whom this operation will succeed. This opinion is in conformity with the much more extensive experience of McKittrick.[15] In none of those having lumbar sympathectomy could it be said that the spread of gangrene was accelerated by the operation.

The following points should be considered in any attempt to improve upon the results presented. Greater cognizance must be taken of anatomic variations in the sympathetic tracts. These variations as shown by Yeager and Cowley,[18] may inadvertantly cause the excision of an inadequate number of ganglia. Cox[3] states that excision of L2 and L3 seldom results in complete sympathetic denervation of the extremity. He estimates that a satisfactory sympathetic tracts. This implies of course that a bilateral sympathectomy might salvage some of the disappointing results.

An additional factor that deserves considerable study is the length of time required after sympathectomy to transform a potential collateral bed into a completely functional unit. It is not unusual to note a gradually increasing response often beginning twenty-four to forty-eight hours postoperatively. This delay in beneficial effect combined with the progression of the gangrenous process, which in some cases may be accelerated by the trauma to either the vena cava or the aorta, may explain the failure of this operation to salvage more extremities.

It was enlightening to note the marked insensitivity of the bacteria to the antibiotics. Specifically, in the four patients in whom antibiotic sensitivity tests were utilized, there was noted complete resistance to penicillin. In addition, two of these patients did not respond to any of the commonly used antibiotics as revealed by the aforementioned test. This was in agreement with the clinical findings.

In the evaluation of additional weapons in the strife against the sequelae of this progres-

sive disease one is impressed with the importance of all the components involved. Every effort must be made to preserve and to increase the circulatory balance. This can be accomplished by simultaneously attacking the inflammatory elements in the pathologic condition while endeavors are directed toward the vascular supply. As mentioned previously lumbar sympathectomy in this series was not utilized in an orderly fashion. In addition the value of early adequate incision and drainage and débridement in the care of these people does not appear to be fully appreciated. The dry-appearing patch of gangrene or granulation tissue most often masks very extensive necrosis and slough of the underlying tissues. This in turn produces a vicious cycle, as the poor circulation of the tissue is further impeded by inflammatory edema and vascular thrombosis. The utilization of the proper antibiotic is of the greatest importance in controlling the bacterial factor.

It is suggested that lumbar sympathectomy to include L1, 2 and 3 preferably be combined with early adequate incision and drainage. At that time cultures and antibiotic studies will enable the selection of the proper antibiotic. Lumbar sympathectomy should be utilized on the uninvolved extremity as soon as it is practicable in the course of the patient's hospitalization.

SUMMARY

1. Lumbar sympathectomy, as it is commonly performed, will not limit the extension of gangrene in advanced arteriosclerotic peripheral vascular disease.

2. The operation appears to be helpful in delineating the site of amputation below the knee.

3. Anatomic and antibiotic considerations are mentioned.

4. A suggested plan for the care of these patients is briefly presented.

REFERENCES

1. Atlas, L. N. Lumbar sympathectomy in treatment of selected cases of arteriosclerosis. *Am. Heart J.*, 22: 75, 1941.

2. Blaine, A. M. and Campbell, K. N. Lumbar sympathectomy for arteriosclerosis obliterans. *Surgery*, 25: 950, 1949.

3. Coller, F. A., Campbell, K. N., Harris, B. M. and Berry, R. E. I. The early results of sympathectomy in far advanced arteriosclerotic peripheral vascular disease. *Surgery*, 26: 30, 1949.

4. Cox, J. W. Objectives of sympathectomy in the treatment of peripheral vascular disease. *Surgery*, 26: 30, 1949.

5. DeBakey, M. E., Creech, O. and Woodhall, J. P. Evaluation of sympathectomy in arteriosclerotic peripheral vascular disease. *J. A. M. A.*, 144: 1227, 1950.

6. Edwards, E. A. and Crane, C. Lumbar sympathectomy for arteriosclerosis of the lower extremities. *New England J. Med.*, 244: 199, 1951.

7. Freeman, N. E., Leeds, F. H. and Gardner, R. E. Sympathectomy of obliterative arteriol disease; indications and contraindications. *Ann. Surg.*, 126: 873, 1947.

8. Frymark, W. B. and Sullivan, J. M. Lumbar sympathectomy for arteriosclerotic peripheral vascular disease. *Ann. Surg.*, 138: 759, 1953.

9. Gerber, L., McCune, W. S. and Eastman, W. Lumbar sympathectomy for arteriosclerotic gangrene. *Arch. Surg.*, 59: 1234, 1959.

10. Jemerin, E. E. Sympathectomy in peripheral arteriosclerosis. *Ann. Surg.*, 129: 65, 1949.

11. Julian, O. C. and Shabert, E. J. Lumbar sympathectomy in peripheral vascular disease. *Arch. Surg.*, 61: 804, 1950.

12. Kirschner, P. A. Limitations of sympathectomy in far advanced peripheral sclerosis. *Ann. Surg.*, 133: 293, 1951.

13. Lee, R. M., Krauskoph, F. F. and Lilly, G. D. Evaluation of lumbar sympathectomy. *South. M. J.*, 42: 864–869, 1949.

14. Lowenberg, R. I. and Morton, D. E. Anatomic and surgical significance of the lumbar sympathetic nervous system. *Ann. Surg.*, 133: 525, 1951.

15. McKittrick, L. S., McKittrick, J. B. and Risley, T. S. Transmetatarsal amputation for infection or gangrene in patients with diabetes mellitus. *Ann. Surg.*, 130: 826, 1949.

16. Smith, R. G., Gullickser, M. and Campbell, D. A. Some limitations of lumbar sympathectomy in arteriosclerosis obliterans. *Arch. Surg.*, 64: 103, 1952.

17. Telford, E. D. and Simmons, H. T. Sympathectomy in peripheral arteriosclerosis. *Brit. M. J.*, 1: 386, 1946.

18. Yeager, G. H. and Cowley, R. A. Anatomical observations on the lumbar sympathetics with evaluation of sympathectomies in organic peripheral vascular disease. *Ann. Surg.*, 127: 953, 1948.

Subtotal Cholecystectomy in Acute Cholecystitis

GORDON F. MADDING, M.D., *San Mateo, California*

SURGICAL management of patients with acute cholecystitis has been and continues to be a subject of considerable controversy. Whether surgery should be carried out when the diagnosis is made or whether a period of symptomatic therapy with delay of operation to a later time is desirable are the current schools of thought. In the surgical treatment of acute cholecystitis not only the time but also the type of procedure to be used varies.

Cholecystectomy has found favor in the treatment of acute cholecystitis by many, while the mortality and morbidity often seen in association with cholecystostomy has been cited by others.[1] The choice in the selection of the type of surgical procedure to be used must be based upon an appraisal of the patient's ability to tolerate any operation and the hazards to the biliary tree when carried out in an operative field in which all normal anatomy is obscured, particularly one in which anatomic variations are so frequent. As recently pointed out by Holman,[2] the number of operative injuries in gallbladder surgery effecting the common and hepatic bile ducts and requiring complicated and frequently disappointing operations for their correction has become truly appalling. Because of the surgical hazard with cholecystectomy when used in the treatment of all cases with acute cholecystitis, resort is often made to the more simple operation of cholecystostomy. The objections to this procedure are the increased morbidity and the frequent need for further biliary tract surgery. In a report of cases by Judd and Priestley,[3] in whom cholecystostomy has been carried out, it was found that 17 per cent of this group required further surgical intervention for disease in the biliary tract. Cattell[4] reported a recurrence of symptoms in 71.7 per cent of cases in which cholecystostomy was carried out. Buxton and Coller[1] found in their series, in which cholecystostomy was used as the initial operation, that more than 50 per cent required further biliary tract surgery.

In contrast to the general trend of more radical surgery in the treatment of acute cholecystitis, as expressed in today's surgical writings,[5–8] I would like to emphasize the merits of a conservative operation, subtotal cholecystectomy, which is a modification of partial cholecystectomy. Subtotal cholecystectomy is to be considered only as a replacement for cholecystostomy when the latter procedure is utilized because of the technical hazards involved in carrying out total cholecystectomy.

TECHNIC OF OPERATIVE PROCEDURE

The gallbladder is exposed by an incision, preferably one paralleling the ribs of the right upper subcostal region. This may be accomplished either after the method of Kerr (Fig. 1A), which has recently been brought to our attention by Holman,[2] or by an extension of the lateral oblique incision of Singleton,[9] in which the right rectus sheath and muscle are divided. (Fig. 1B.) After the peritoneal cavity has been opened and the gallbladder walled off its fluid contents are aspirated. This is especially valuable if the gallbladder is greatly distended, for the surface area is sufficiently reduced to make dissection easier and the likelihood of spillage is reduced. An incision may then be made from the fundus to within 1 cm. of the cystic duct and all stones removed, particularly the one creating the obstruction of the cystic duct. No attempt is made to isolate the cystic duct or artery in the presence of the brawny induration in the hepatoduodenal ligament. When, following removal of all stones, the redundant flaps of the gallbladder are trimmed off at the liver bed attachment, the procedure has been designated in the literature as partial cholecystectomy, an operation first described in 1899.[10] When the gallbladder is dissected in a retrograde fashion from the surface of the liver proper down to within 1 cm. of the cystic duct, the method will be referred to as "subtotal cholecystectomy" and is the preferable procedure. Subtotal cholecystectomy is a less time-consuming and more effective operation than partial cholecystectomy

for it incorporates more of the advantages of total cholecystectomy. It reduces the amount of inflammatory tissue remaining and consequently decreases the amount of drainage postoperatively. Any method which leaves the entire posterior gallbladder wall attached to its gallbladder bed and depends upon surface treatment to destroy the residual infected tissue will be found wanting and associated with an increased period of convalescence because of the prolonged drainage. After a subtotal cholecystectomy has been carried out the gallbladder fossa is treated as though a total cholecystectomy had been used. As a rule this fossa bleeds when the gallbladder has been dissected from the liver surface proper and it is frequently necessary temporarily to apply a warm moist pack to the gallbladder fossa or place a piece of gelfoam or oxycel into this area. After using either of the latter two agents, the liver edges are approximated over the hemostatic agent by means of a running interlocking stitch of fine atraumatic catgut. For the destruction of any mucosa, which may remain in the cuff of gallbladder left attached to the cystic duct, one of a number of methods are available. Such mucosa, however, is not often encountered, for as a rule it has been destroyed by the existing acute inflammatory process. Where mucosa persists it may be removed by means of curettage, application of tincture of iodine, phenol or after the method of Thorek,[11] who uses electrosurgical coagulation in his partial cholecystectomies. It is my preference to use phenol, followed by alcohol and saline for this purpose. The phenol and alcohol are readily available and easily applied by means of cotton applicators, after which the area is bathed with a small amount of saline solution. A Penrose drain is then placed into the stump of gallbladder which remains, this gallbladder remanent usually not exceeding 1 cm. in diameter. The cuff is then closed about the drain with interrupted catgut sutures. (Figs. 2 and 3.) Other drains are placed and these in turn are brought out the lateral angle of the wound where a subcostal type of incision has been used. Where a right rectus incision has been utilized, drainage should be accomplished through a stab wound placed in the right subcostal region in the anterior axillary line. Adequate drainage is a most important step in further reducing the inflammation and narrowing of the extra hepatic bile ducts

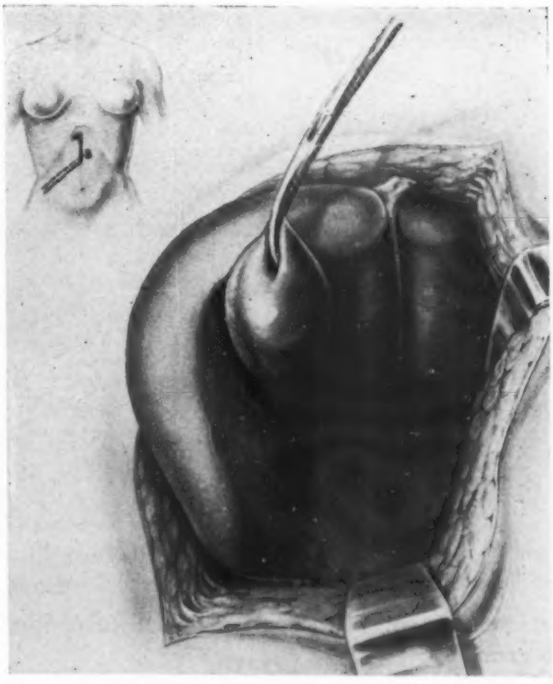


FIG. 1. Showing exposure as obtained through insert A, Kerr incision, and B, Singleton incision.

by accumulation of infected exudate and bile in this area. The omentum is carefully placed and at times sutured in between the duodenum and gallbladder fossa to reduce the formation of postoperative adhesions which may involve the duodenum. The abdominal wall is then closed in the usual fashion. For this purpose, it is my practice to use chromic catgut in the posterior rectus sheath and peritoneum and interrupted non-absorable sutures in the external rectus sheath, median raphe and external oblique muscle and fascia. (Fig. 3.)

CASE REPORTS

CASE 1. C. A. B., a white woman, age forty, was admitted to the hospital on February 18, 1948, with a diagnosis of acute cholecystitis of three days' duration. Operation was carried out and a gangrenous gallbladder found. Because of the marked amount of inflammatory reaction about the gallbladder and in the hepatoduodenal ligament a subtotal cholecystectomy was carried out. The patient's postoperative course was uneventful. She was discharged from the hospital on March 2, 1948, and was last seen September 1, 1953, having had no trouble since that time. The pathologic report was gangrenous cholecystitis with stones. Her reason for reporting to the clinic on Septem-

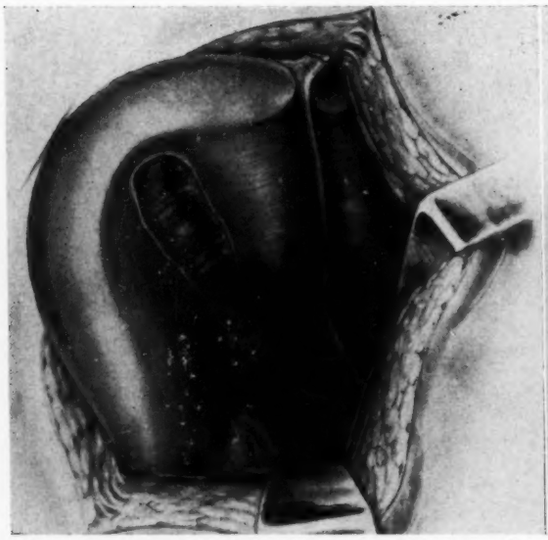


FIG. 2. Showing gallbladder removed and cuff of gallbladder remaining.

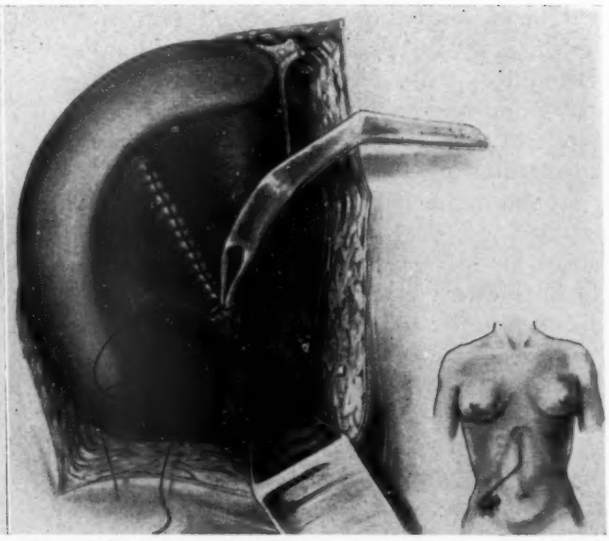


FIG. 3. Showing gallbladder fossa closed. Drain in gallbladder cuff remaining.

ber 1st was for a left sciatica which responded to exercises.

CASE II. L. H., a forty-six year old Negro man, was admitted to the hospital on April 2, 1948, with an intermittent history of several months' duration of typical gallbladder disease. The last ninety-six hours the patient had had severe pain in the right upper abdominal quadrant, with chills and fever but no jaundice. At surgery on April 3rd an acute gangrenous cholecystitis was found. Because of the marked amount of inflammatory reaction in and about the gallbladder and hepatoduodenal ligament a subtotal cholecystectomy was performed. There was some biliary drainage for two days but the patient was discharged from the hospital on April 11th. Pathologic report was acute cholecystitis with stones.

CASE III. J. H. D., a seventy-two year old white man, was admitted to the hospital August 4, 1950, with a diagnosis of intestinal obstruction. Conservative treatment was carried out until a diagnosis of probable empyema of the gallbladder was made. On August 10th the patient was taken to surgery and through a right upper subcostal incision an acute condition of the gallbladder with empyema was found. There was a rather marked ileus. The omentum was fixed about the gallbladder and there was considerable pericholecystitis and perihepatitis secondary to a small perforation in the gallbladder wall. The hepatoduodenal ligament was markedly edematous and the foramen of Winslow was closed. In the absence of a history of jaundice and the marked amount of inflammatory reaction with distortion of the local structures, a subtotal cholecystectomy was carried out. The patient did well, although while in the hospital some urinary difficulty developed secondary to hypertrophy of the prostate, and a transurethral prostatectomy became necessary. All drains were removed from the gallbladder incision, however, on the fourth postoperative day. The patient was discharged from the hospital September 19th, forty-six days postoperatively. Pathologic report was gangrenous cholecystitis with stones. He was last seen in the office three years later, having had no trouble with his gastrointestinal or biliary tract and was seen in the Urologic Department because of some slight urinary difficulty.

CASE IV. R. C., a twenty-seven year old white woman, was admitted to the hospital on August 11, 1953, with a diagnosis of perforated peptic ulcer or acute cholecystitis of three days' duration. Because of the question of perforated duodenal ulcer, stomach and duodenal x-rays were made, which were negative. The acute symptoms persisted. On August 14, 1953, the abdomen was opened through a right upper subcostal incision and the omentum was found attached to the gallbladder which was markedly distended. The omentum was freed from the gallbladder proper and subtotal cholecystectomy carried out in a retrograde fashion, leaving approximately 1 cm. cuff of gallbladder. The patient's postoperative course was un-

eventful. There was slight biliary drainage for three days and the drains were completely removed after the sixth postoperative day. The patient was discharged on the ninth postoperative day. When last seen six months later the patient was in good health.

COMMENTS

In the author's hands results of subtotal cholecystectomy, in selected cases, have been gratifying. Because the major focus of stone formation, which is the obstructing agent in approximately 95 per cent of all cases of acute cholecystitis, has been removed, it is believed that cholecystectomy has much to recommend its usage as a procedure to replace cholecystostomy. The latter procedure should be reserved for that rare patient whose condition is so precarious that anything more than drainage of the acutely inflamed gallbladder under local anesthesia would be found contraindicated. Subtotal cholecystectomy will find its greatest usefulness in cases of acute suppurative or gangrenous cholecystitis, with or without empyema of the gallbladder, especially where the cystic and common bile ducts rest in an edematous, friable and infected field in which all local anatomy is obscured.

It is well to remember that anatomic variations in the region of the gallbladder and biliary ducts are many and when these are further obscured by any pathologic process the technical hazards in carrying out total cholecystectomy are increased. In many of these cases, subtotal cholecystectomy, with removal of the obstructing agent in the cystic duct, will obviate the need for performing cholecystostomy and thus reduce the need for further biliary tract surgery.

A great deal has been said about the residual cystic duct stump in its relation to the postcholecystectomy syndrome. As Ray[12] has pointed out, it would be better if more was said about the too short cystic duct resulting in stricture or interruption of the extrahepatic bile ducts. Estes[13] found no remanent of the gallbladder in his cases of acute cholecystitis treated with partial cholecystectomy who were re-operated upon for various reasons.

SUMMARY

When feasible, total cholecystectomy is still the operation of choice in the surgical treatment of acute gallbladder disease and subtotal cholecystectomy should not be considered to supplant it. However, when complete removal cannot be safely accomplished, subtotal cholecystectomy recommends itself for consideration to obviate the use of cholecystostomy. Subtotal cholecystectomy incorporates the advantages of total cholecystectomy and has none of the drawbacks of cholecystostomy. A procedure such as cholecystostomy, which is followed by the need for further biliary tract surgery in such a large percentage of cases, leaves much to be desired. In all, excepting the extreme bad risk case in which a drainage operation only is permissible, subtotal cholecystectomy has proved, in my hands, a safe operation, yielding just as satisfactory permanent results as complete cholecystectomy.

Four cases are reported with no mortality and a morbidity comparable to that following total cholecystectomy in the treatment of chronically infected gallbladder with cholelithiasis.

REFERENCES

1. Buxton, R. W., Ray, D. K. and Coller, F. A. Acute cholecystitis. *J. A. M. A.*, 146: 301–307, 1951.
2. Holman, E. An incisional approach for cholecystectomy and choledochotomy designed to reduce injuries to the common duct. *Surg., Gynec. & Obst.*, 97: 344–352, 1953.
3. Judd, E. S. and Priestley, J. T. Ultimate results from operations on biliary tract. *J. A. M. A.*, 99: 887, 1932.
4. Cattell, R. Cholecystitis. *Ann. Surg.*, 8: 930–941, 1928.
5. Heuer, G. J. Treatment of gallstone disease. *Internat. Clin.*, 3: 121–134, 1940.
6. Dunphy, J. E. and Ross, F. P. Studies in acute cholecystitis-cholecystostomy indications and technic. *New England J. Med.*, 242: 359–362, 1950.
7. Glenn, F. Surgical treatment of acute cholecystitis. *Surg., Gynec. & Obst.*, 90: 643–649, 1950.
8. Fallis, L. S. and McClure, R. D. Acute cholecystitis—review of 320 cases. *Surg., Gynec. & Obst.*, 70: 1022, 1940.
9. Singleton, A. L. and Blocker, T. G., Jr. Problem of disruption of abdominal wounds and post operative hernia; review of 9,000 consecutive abdominal incisions. *J. A. M. A.*, 112: 122, 1939.
10. Mayo, W. J. and Mayo, C. H. Collection of Papers Published Previous to 1909. Pp. 348–355. Philadelphia, 1912. W. B. Saunders Co.
11. Thorek, M. Experience with electrosurgical obliteration of the gallbladder. *J. A. M. A.*, 154: 738–740, 1954.
12. Ray, D. K. Discussion of Paper by Buxton, R. W., Ray, D. K. and Coller, F. A.
13. Estes, W. L., Jr.: Acute gangrenous cholecystitis and the use of partial cholecystectomy in its treatment. *Am. J. Surg.*, 40: 197–204, 1938.

New Concept of Total Hysterectomy and Anatomy of the Cervix

MORRIS JOSEPH, M.D., *Passaic, New Jersey*

DURING the past ten years total hysterectomy, either by the vaginal or abdominal route, has gradually increased in popularity. Primarily, the object of this operation to include the cervix was designed to eliminate existing disease of this organ. At the same time this procedure obviated the potential carcinoma that involves the cervix in about 2 per cent of all cases after simple subtotal hysterectomy has been performed.

For many years Richardson[1] has strongly opposed any operative procedure on the female genitalia which would destroy the important fibrous cervical ring, acting as a fulcrum, that supports the cardinal ligaments. Crossen[2] and others have also stressed this danger and the incidence of complete prolapse following these procedures. In total hysterectomy, regardless of the abdominal or vaginal route, this cervical ring is removed. Simply bringing the cardinal ligaments and round ligaments together, in the closure of the pelvic floor, does not supply a satisfactory substitute.

As women grow older the strong resilient elastic tissue of the pelvis and vagina often becomes parchment-like in character. This tissue has very poor supportive qualities and a very distressing prolapse ensues. Because of the nature of the tissue a satisfactory repair is often difficult, if not impossible.

For this reason this type of hysterectomy with the use of a special knife has been designed. This procedure not only eliminates the defects already mentioned but also removes all the necessary cervical tissue as well as the mucosal channel and the body of the uterus. In this way all existing or potential cancer areas are completely eradicated.

PROCEDURE

Most of our patients are prepared with spinal anesthesia, often supplemented with very light pentothal intravenously. The addition of this light pentothal produces a mild state of unconsciousness. The complete relaxation of the patient, however, is produced by the spinal. The patient is placed in position for abdominal hysterectomy.

The routine supracervical hysterectomy is performed, except that the cervix is not completely amputated. The muscular portion at the uterocervical junction corresponding to the internal os is incised and circumscribed down to the fibro-elastic tube, which completely encloses the mucosa of the cervix. This structure was discovered in our early cases and presented an entirely new concept in the anatomy of the cervix. It was this fibro-elastic avascular tube that facilitated the complete enucleation of the mucosa of the cervical canal, without entering the canal and with little or no bleeding. This tubular structure is left intact and remains attached to the corpus uteri. The dissection is continued downward to and including the external os.

A small or larger area of the squamous lining of the cervix, circumscribing the external os, may be included. If this is done, it is advisable to do it vaginally before the abdominal procedure is begun. The reason for this sequence is that at times after the squamous covering is removed, little or no bleeding is evident. However, after the abdominal portion of the operation is performed, the blood supply from the uterine artery is limited entirely to this small segment of cervix. With a sudden and abundant increase in the arterial pressure what appeared like little or no bleeding at the cervical tip suddenly may be converted into an alarming hemorrhage. There have been two such cases in our series. This complication can really be of major proportion.

When it is deemed advisable to excise the squamous epithelium of the cervix because it is manifestly diseased, cystic or scarred from previous lacerations, it should be done. Then the cervical phase of the operation is carried out initially and the cervical branches of the uterine

FIG. 1. Specimen of total hysterectomy including external os.

artery must be adequately secured by a suture ligature. It is also preferable to cover the small remaining raw area by undermining the cervical reflection of the vaginal mucosa sufficiently and placing a few small sutures to cover this area. After the cervical stump is drawn high into the vaginal vault and anchored in the pelvis, following the abdominal excision, control of hemorrhage becomes extremely difficult. This point cannot be stressed too strongly. One of our cases presented such a problem recently.

It is our belief that once the entire cervical mucosa is removed to include the external os, there is little to fear from future carcinoma of the cervix. Once the secretory element of the cervix is removed there should be no hazard from carcinoma. The resulting stump is simply a solid muscular column serving as a hitching post.

ANATOMY OF THE CERVIX

It seems strange and surprising that after all these years a simple structure such as the cervix is found inadequately described in any of our anatomy texts. The fibro-elastic tube encasing the cervical mucosa is what facilitates and makes possible this new concept of total hysterectomy. It dissects out like a miniature

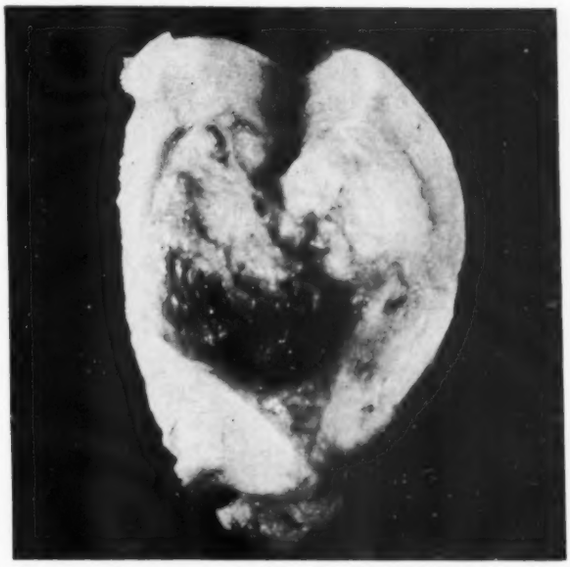


FIG. 2. Same case. Adenocarcinoma within the fibroid. No invasion below internal os or adnexae.

esophagus and because of its avascularity the procedure becomes very simple; with a little practice it should consume less time than the standard total hysterectomy. The "cone excision" of the cervical canal without entering the canal was first suggested by Matthews[8] in his description of the Sturmdorf operation.

One of our very recent patients* showed evidence of early adenocarcinoma in a fibroid uterus. There was no invasion below the internal os of the cervix. The excision of the cervical canal in this case might have been very timely. (Figs. 1 and 2.)

COMMENTS

In performing this type of hysterectomy everything that the routine standard total hysterectomy accomplishes is made possible. The anatomy of the cervix likewise makes possible its preservation for its very important supporting purpose. This also allows the normal preservation of the pelvic floor and spares disabling the patient in later years. All potential cancer is eliminated and at the same time its splendid supporting qualities are preserved.

The operating time element, if anything, is reduced. With a little practice the technic is simpler than the standard total hysterectomy. The very distressing prolapse and other com-

* This patient was a thirty-seven year old woman who had bled steadily for one month. Fibroid uterus was diagnosed. She had never been pregnant.

plications which follow in many cases of the standard operation are greatly reduced.

Of course it is clearly understood that before any vaginal or abdominal procedure has been undertaken every precaution to rule out malignancy is first performed. Both biopsy and smears should be taken to rule out the slightest evidence of incipient malignancy.

TABLE 1
DIFFERENTIAL IN COMPLICATIONS BETWEEN TOTAL VS. SUBTOTAL HYSTERECTOMY (NEW TYPE OF TOTAL HYSTERECTOMY)

Authors	Total Hysterectomy		Subtotal Hysterectomy	
	Number	Per cent	Number	Per cent
H. D. Adams[3] 30 cases of prolapse...	12	....	7	....
T. W. Adams[4] 436 cases of unilateral ureteral injury.....	312	65.4	57	12.3
97 cases of bilateral ureteral injury.....	67	69.7	7	7.0
J. C. Weed and C. Tyrone[5] 52 cases of enterocele..	27	....	7	....

The difference in complications following the standard total versus this new type of hysterectomy is exemplified in the statistics shown in Table 1.

CONCLUSIONS

1. This new concept of total hysterectomy was originally described as a vaginal-abdominal procedure.[6] The special knife[7] has greatly facilitated this operation.

2. The present modification simplifies the technic and reduces the time element.

3. It has all the advantages of the presently accepted standard procedure, without its disadvantages.

4. A new concept of the structure of the cervix has facilitated the development of this operation.

REFERENCES

1. RICHARDSON, E. H. Composite operation. *Am. J. Obst. & Gynec.*, 34: 815, 1937.
2. CROSSEN, H. S. and CROSSEN, R. J. Operative Gynecology, 6th ed. St. Louis, 1948. C. V. Mosby Co.
3. ADAMS, H. D. Total colpocleisis for pelvic eventration. *Surg., Gynec. & Obst.*, 92: 321–324, 1951.
4. ADAMS, T. W. Ureteral injury during gynecologic surgery. *West. J. Surg.*, 51: 305–324, 1943.
5. WEED, J. C. and TYRONE, C. Enterocele (an analysis of 52 cases). *Am. J. Obst. & Gynec.*, 60: 324–332, 1950.
6. JOSEPH, M. New vaginal-abdominal hysterectomy with special knife. *West. J. Surg.*, 58: 227–228, 1950.
7. JOSEPH, M. New knife for cervical cancer. *J. M. Soc. New Jersey*, 46: 345, 1949.
8. MATTHEWS, H. B. Electric cautery vs. Sturmdorf operation. *J. A. M. A.*, 87: 1695, 1926.

Diagnosis and Treatment of Pulmonary Tuberculosis

ROGER S. MITCHELL, M.D., *Trudeau, New York*

From Trudeau Sanatorium of the Trudeau-Saranac Institute, Trudeau, New York.

PULMONARY tuberculosis is a chronic, relapsing disease characterized by focal destruction of lung tissue and frequently by poor correlation between the actual extent of the disease process and the severity of the clinical picture.

The symptoms of pulmonary tuberculosis can be divided into six categories. The most common symptom group is the catarrhal: cough, expectoration, wheeze and dyspnea. The next most common is the constitutional, with temperature elevation, night sweats, dyspepsia, loss of weight and strength, arthralgia, anorexia, nausea, vomiting and diarrhea. The fever of pulmonary tuberculosis is commonly higher in the evening than in the morning. Hemoptysis is a common early as well as late symptom of the disease. Hemoptysis in pulmonary tuberculosis usually persists for three to several days; the blood is usually incompletely mixed with sputum. It is usually, but not always, a manifestation of active disease. Episodes of "grippe" or influenza-like illness are quite common throughout the course of tuberculosis. They are characterized by malaise, fever, prostration, sore throat and followed by cough and expectoration which fail or are slow to improve. Anyone with such symptoms should have a chest roentgenogram without fail. Pleurisy is common in tuberculosis, but unless accompanied by a pleural effusion is by no means characteristic of the disease. In fact, most dry pleurisies are non-tuberculous in origin. The patient sometimes presents the clinical or roentgenographic picture of pneumonia, neither of which can be distinguished from a non-tuberculous pneumonic process except on bacteriologic grounds. Lastly, it should not be overlooked that many patients with active pulmonary tuberculosis are either free of symptoms or deny them until treatment has been in effect for some time; then one may become aware of easy fatigability or malaise in retrospect. Euphoria has been described as a common symptom but is by no means characteristic of this disease.

Physical signs in pulmonary tuberculosis are of relatively limited importance. Amphoric breath sounds, consonating rales and hyperresonance, the classic signs of cavity, are not reliable. Posttussive rales in one or both apices may or may not be present. Rales may be present in both apices in the presence of partially decompensated mitral stenosis. Rales are frequently heard in the presence of old, burned out, clinically inert disease and are frequently absent in the presence of progressive, even cavitary disease involving the entire apex. Signs of pleural effusion and consolidation are apt to be much more reliable than rales. Signs of bronchial obstruction—expiratory wheeze aggravated by lying in the lateral recumbent position on the affected side—are quite reliable. Emphysema may be diagnosed with considerable accuracy from the distant breath sounds, long expiratory phase and inability to increase the intensity of the respiratory murmur on rapid forced breathing. Other signs worth looking for are lymphadenitis, especially in the neck, draining sinuses, especially in the rectal region, muscle wasting (myedema) and a nodule in the epididymis.

It has been said that there is no roentgenographic pulmonary infiltration characteristic of tuberculosis. However, fluffy mixed with stringy densities, especially in the upper lung fields with one or more areas of rarefaction and/or evidence of pulmonary contraction with mediastinal deviation and the like, may be considered tuberculous until proven otherwise.

A positive tuberculin test is practically essential for the diagnosis of tuberculosis, although in rare instances, as in the presence of overwhelming tuberculous or other infections, or in the presence of prostration from any cause, the tuberculin test may be negative in the presence of active tuberculous infection. There is a one to three-week lag between the time of infection and the development of a positive tuberculin reaction.

The diagnosis of pulmonary tuberculosis is greatly aided by the finding of acid-fast bacilli in the sputum or by the recovery of Mycobacteria tuberculosis by culture of sputum concentrates or gastric washings on appropriate culture media. It should not be overlooked that gastric washings in particular and tap water may contain non-pathogenic acid-fast bacilli, at least in small numbers. In the absence of confirmation of the diagnosis by bacteriologic means one should not hesitate to make a diagnosis of pulmonary tuberculosis if supported by the history, chest roentgenograms and other findings. Most advanced and at least 60 per cent of minimal tuberculosis will yield positive bacteriologic findings on repeated careful examination. When sputum is not available, several gastric washings should be obtained. The gastric washing should be performed before digestion has started in the morning.

Differential diagnosis may well be studied from the standpoint of other causes of the diagnostic signs of tuberculosis. First, hemoptysis is most commonly caused by bronchiectasis in children and by carcinoma in patients over forty-five, whereas tuberculosis is probably the most common cause in the eighteen to forty-five year old age group. Other common causes of hemoptysis include heart failure, pulmonary infarction, pneumonia, bronchial adenoma, foreign body, fungus disease and abscess. Pleurisy with effusion must be considered tuberculous unless proven otherwise. Other causes of this syndrome include heart failure, fungus diseases, pulmonary infarct, non-tuberculous pneumonia, Loeffler's syndrome and certain other rare diseases.

Other major causes of weight loss and easy fatigability are hyperthyroidism, diabetes, malignancy and psychoneurosis.

TREATMENT

The treatment of pulmonary tuberculosis today may be divided into five parts:

Chemotherapy. Every patient with active pulmonary tuberculosis considered in need of any treatment today should receive chemotherapy. In other words, there seems little justification for the use of rest alone or rest with collapse and/or resection without combined drug therapy.

The best drug regimens are: (1) streptomycin (or dihydrostreptomycin or streptoduocin—equal parts of streptomycin and dihydrostreptomycin), 1 gm. intramuscularly twice weekly or daily, plus para-aminosalicylic acid (PAS), 12 gm daily or its equivalent (16 gm.) of sodium PAS, taken in three divided doses immediately after meals by mouth; and (2) isoniazid, 100 mg. three times daily by mouth, plus PAS in the same dosage. Streptomycin (or dihydrostreptomycin or streptoduocin) plus isoniazid is less desirable because, while being no better, it combines the two most effective agents in one regimen. A regimen of all three is used in meningitis and miliary tuberculosis but is considered unnecessary in most pulmonary tuberculosis. PAS alone has little value. Isoniazid alone may prove effective in selected cases but its use is not encouraged.

When patients have received streptomycin, PAS or isoniazid therapy previously, pretreatment drug sensitivity tests are indicated to determine the best regimen. While awaiting the outcome of these tests in threatening situations it is advisable to use all three drugs daily. When drug sensitivities are known, give the other two drugs when resistance to the one is present. When resistance to two or three drugs is found, all three drugs should be used. In this situation some prefer a regimen of viomycin, 2 to 3 gm. intramuscularly twice weekly and oxytetracyline, 2 gm. daily by mouth.

Recently pyrazinamide, 3 gm. daily by mouth, combined with isoniazid, 300 mg. daily by mouth, has been found to be an encouraging

experimental regimen. Used in mice this regimen was found to have a bactericidal action against M. tuberculosis in contradistinction to all other drugs and combinations in use whose action in the host is bacteriostatic.

The important principles of antituberculosis chemotherapy are: (1) seldom if ever use one drug; (2) avoid interruptions in treatment insofar as possible; (3) continue treatment for no less than twelve to eighteen months and at least six months beyond the attainment of the therapeutic objective of disappearance of all cavities, conversion of sputum and/or gastric washing cultures, freedom from symptoms and stability of serial x-rays.

The emergence of drug resistance is an ever present problem. The risk of drug resistance is reduced by avoidance of interruptions, especially interruptions of one drug only of a two-drug regimen, and by the combined use of two or more drugs. Resistance is apt to appear when cavities fail to close. Hence integration of collapse and/or resection with chemotherapy plays an important part in the ultimate success of treatment. There is good general correlation between *in vivo* and *in vitro* drug resistance.

The toxicity of these drugs presents an occasional problem. Streptomycin commonly causes dizziness, and dihydrostreptomycin deafness; both are injuries of the eighth cranial nerve. Streptoduocin, a half and half mixture of streptomycin and dihydrostreptomycin, was devised in an attempt to minimize these twin toxicites. Reduction of dosage to 0.5 gm./day, especially in patients past fifty, is another effective means of reducing ototoxicity. Renal damage by the streptomycin drugs is occasionally reported. PAS rather commonly causes gastro-intestinal upsets characterized by anorexia, abdominal cramps, vomiting and loss of weight. These effects may be minimized by reassuring the patient, by trying different ways of administering the drug, by making sure it is taken immediately after meals with plenty of water and by judicious reduction in dosage. Isoniazid seldom produces serious toxicity except for occasional peripheral neuritis which, incidentally, is quite recalcitrant to treatment. Viomycin is capable of causing serious liver and kidney disturbance but this is unlikely with the 2 gm. dose twice weekly. Two grams of oxytetracyline daily is quite apt to cause gastro-intestinal disturbance. All of these drugs, particularly PAS and the streptomycin drugs, may cause a hypersensitivity reaction. The symptoms of hypersensitivity are usually skin eruption, high fever, prostration, nausea, vomiting, diarrhea, lymphadenopathy and occasional leukopenia. When true hypersensitivity is present, simultaneous desensitization to all drugs being used is wise. In so doing parallel doses of drugs are always used; i.e., full doses of one drug are not given while another drug is being given in infinitesimal doses. The risk of drug resistance is thereby reduced. Desensitization to streptomycin is frequently started with 1 mg. intramuscularly daily; 1 gr. of PAS three times a day and 1 mg. of isoniazid are likewise used. The doses are changed at two to three-day intervals by increasing the dose by 50 to 100 per cent. Dihydrostreptomycin and streptomycin may be substituted for each other in case of hypersensitivity to one.

Rest Therapy. All patients with active pulmonary tuberculosis are advised to take rest therapy. Rest treatment acts by promoting the natural healing powers of the body. Its effectiveness is unquestioned. How much is needed in the individual case, however, is the source of considerable disagreement. It acts by reducing lung motion and size, by stimulation of the bodily resistance against infection and promotes patient education.

The need for rest therapy has been materially reduced by the advent of modern chemotherapy. Some mild cases may need no rest but this has not yet been clearly established.

The educational value of resting, preferably in a sanatorium for at least a few months, is very important. Education is vital when one considers that unpleasant medication, collapse and other treatments must be taken long after the disappearance of all signs and symptoms of active disease. Instruction in the prevention of spreading the disease, especially good cough discipline, is another essential part of the patient's education.

At the beginning of treatment it is recommended that rest therapy be rather strict with no more than two or three bathroom privileges permitted; in the presence of fever or prostration strict bedpan rest is sometimes advised. As soon as the patient has become adjusted to resting and in the absence of unfavorable symptoms or signs, permission is frequently given to be out of bed for two to four hours a day for

meals, bathroom privileges and simple occupations. In the case of minimal tuberculosis, gradually increasing walking exercise outdoors may be prescribed three to five months after beginning rest therapy. In advanced disease permission to take outdoor exercise is postponed for five to nine months or more. With favorable response to treatment, patients with minimal tuberculosis may be permitted to resume part-time work in from nine to ten months and full-time work in from twelve to eighteen months. In patients with more advanced disease, work is delayed according to the individual personality, maturity and response to treatment. Most patients today resume their work while still receiving drug therapy. It should be emphasized, however, that this outline of rest therapy applies to the average uncomplicated case. Less rest is used in the presence of diabetes, emphysema and old age. Most rest is often prescribed in the young and immature.

Collapse Therapy. This may be divided into the temporary and permanent forms.

Temporary collapse consists of one of three measures:

1. Pneumoperitoneum is the introduction of air into the peritoneal space by means of injections of 500 to 1,800 cc. of air with a needle at a point to the left of the umbilicus at intervals of seven to fourteen days. The air is given to elevate the diaphragm and thereby reduce the volume of air in the lung and encourage collapse of segments containing cavities. It is used in patients with cavities of 2 cm. or more in diameter, regardless of their location. After it is established and if effective, it is continued for one to three years or at least six months, possibly for a year or more after attainment of the therapeutic objective previously described. Complications of pneumoperitoneum are air embolism, mediastinal emphysema, peritoneal fluid and a number of minor disturbances.

2. Pneumothorax is used much less frequently today than formerly and in some places hardly at all, mainly because of the risk of pleural complications—pleural effusion, empyema, bronchopleural fistula—and the likelihood of severe loss of function resulting therefrom. Although these complications commonly appear early, their onset may be delayed months or even years. On the other hand, pneumothorax is a more specific and effective collapse measure than pneumoperitoneum. Because of the aforementioned risks, unpredictable at the outset, the collapse which is intended to be temporary may become permanent. The presence of bronchial disease is a potent source of these serious complications. Pneumothorax, used with modern effective chemotherapy, is proving much safer than previously and may ultimately prove to be effective and essentially free of complications.

Thoracoscopy in search of adhesions is indicated in most cases; adhesion section—pneumonolysis—will be necessary in order to achieve a satisfactory collapse in the majority. Refills are given at from three to forty days in amounts ranging from 50 to 700 cc. The pressure is usually maintained at mildly negative levels and with a partial rather than a total collapse controlled by frequent fluoroscopy. Pneumothorax is usually continued for one year or more after attainment of the therapeutic objective, as in the case of pneumoperitoneum.

3. Phrenic nerve paralysis is very seldom used today. In paralyzing one hemidiaphragm for six to nine months, collapse may occur but often does not; the lung is simply prevented from full distention with each breath in most cases unless supplemented by pneumoperitoneum. Today the procedure may be used as an adjunct to pneumoperitoneum in cases unsuitable for thoracoplasty or resection. The phrenic nerve is crushed in the neck under local anesthesia; in successful cases it should be repeated once or twice after regeneration. Repetition and coincident use of pneumoperitoneum both reduce the likelihood that full return of function will occur. Hemidiaphragmatic paralysis is a mild contraindication for thoracoplasty or pulmonary resection. Complications are mild and infrequent and include paralysis of the wrong nerve and damage to the thoracic duct.

Permanent collapse consists of one of two measures:

1. Thoracoplasty, or the shortening of from five to eleven (usually six to eight) upper ribs on one side, was a well established, highly effective and reliable treatment for pulmonary tuberculosis long before the days of chemotherapy. Because at least mild deformity can hardly be avoided, because it is not possible to perform thoracoplasty by means of any less than two operations, because persistent, usually mild discomfort is difficult to avoid, and because there are now other effective measures to replace it, thoracoplasty is being used less and

less. The fact remains, however, that thoracoplasty stands alone as the single, most effective form of treatment for serious tuberculosis over the long pull to date. The results of chemotherapy and lucite plombage are too recent to permit reliable comparison with thoracoplasty. Thoracoplasty is indicated when a cavity is present in the upper half, principally in the upper third of the lung field. Thoracoplasty is also performed to reduce the size of the hemithorax following large resections and in the treatment of postpneumothorax empyema. Bilateral thoracoplasty can be performed, but not more than a total of eleven ribs on both sides should be shortened even in a candidate with good breathing reserve. Complications include pleural effusion, inadvertent lung tears, wound infection and mediastinal flutter.

2. Permanent collapse is now usually performed by means of either a temporary or permanent lucite plombage. Temporary plombage is the placing of lucite spheres in a space created surgically beneath the upper four to six ribs posteriorly. The lung to be collapsed is displaced medially together with the fascia containing the periosteum peeled from the ribs selected. The space is packed loosely and never under any pressure. After eight to ten weeks new ribs will have been regenerated from the strips of periosteum; the old denuded ribs and the lucite spheres are removed at a second operation. The result is usually indistinguishable from conventional thoracoplasty.

The permanent plombage is accomplished by placing the spheres within a pliofilm bag in a space similar to that previously described, with the exception that only part of the periosteum from each rib is displaced medially; enough periosteum is left on each rib to preserve its viability. In due course, therefore, the patient has two sets of ribs separated by a plastic plombage which is left in permanently. Whether the plombage is left in or removed, the collapse is quite comparable to thoracoplasty. The operative trauma of lucite plombage is even less than thoracoplasty and is simpler for the surgeon to perform. Plombage has the added advantage of avoiding soft chest wall and mediastinal flutter and is therefore applicable to patients who might not be candidates for thoracoplasty from the standpoint of respiratory reserve. Complications include infection of the space, migration of spheres and pleural effusions. Sufficient time has not yet elapsed to permit final evaluation. Caution is advised in evaluating any procedure involving leaving foreign material in the body.

Resection of Pulmonary Tissue. This has become a widely applied, highly effective form of treatment for pulmonary tuberculosis since the advent of effective chemotherapy and as a result of greatly improved surgical technics. The removal of lung tissue may range all the way from an entire lung (pneumonectomy) to lobectomy, segmental lobectomy and subsegmental or wedge resection. The amount of lung tissue to be removed is determined by the amount of involvement and anatomic considerations found at operation.

The selection of patients for resection is determined largely by the persistence of cavity during chemotherapy and/or after collapse, either temporary or permanent. In the presence of pleural infection (empyema), such as that which used to accompany pneumothorax, a pleuropneumonectomy may be performed. This consists of the removal of the lung together with both layers of the pleura and parts of the chest wall at the same time. The complications of pulmonary resection are bronchopleural fistulas (air leaks), empyema, atelectasis, spread of tuberculosis, draining sinuses and surgical mortality. The risk of a segmental resection performed under competent drug coverage is less than 1 per cent today. The mortality risk of lobectomy is in the neighborhood of 1 per cent; for pneumonectomy the risk ranges between 5 and 10 per cent. The risk of complications, on the other hand, is considerably higher, ranging between 5 to 20 per cent, depending upon the extent of the operation and the competence of drug coverage. The question of whether a tailoring thoracoplasty should be performed following the removal of lung tissue is usually determined by the ability of the remaining lung tissue to inflate and fill the thorax. When large amounts of lung tissue are to be removed, the need for thoracoplasty can be determined preoperatively and sometimes performed before the resection. The thoracoplasty is performed not only to prevent overdistention of the remaining lung but also to prevent filling of the pleural space with fluid which may readily become infected.

Other Measures. Cavity drainage is occasionally performed, especially in large apical tension cavities, either with a tube in the cavity (Monaldi) or by an incision into the

cavity, sewing the skin down to its margins so as to keep it open for many months (cavernostomy).

Decortication is removal of the thickened peel which has formed on the pleura. This occurs during the administration of pneumothorax especially when complicated by effusion and after a spontaneous attack of pleurisy with effusion. If there was much tuberculosis in the lung during its collapse with pneumothorax, the chance of improving function with decortication is quite limited unless performed very soon after collapse was initiated. If there has been little or no infection in the collapsed lung, the chance of improving function with decortication is good and not closely related to duration of collapse. In any event, however, decortication may very well help in space filling even if function is not improved.

Extrapleural pneumothorax is occasionally practiced where an intrapleural pneumothorax space cannot be developed and where some other measure such as thoracoplasty or resection is refused or unavailable. An extrapleural space is created over the area in need of collapse by a major surgical operation. This space is then filled with air and the air is kept in the space under positive pressure over a period ranging from two to four years. Frequently extrapleural pneumothorax must be replaced by a permanent thoracoplasty collapse when it is abandoned.

SUMMARY

1. The essential features of the diagnosis of pulmonary tuberculosis are pulmonary infiltration by chest roentgenogram, the finding of acid-fast bacilli in concentrated sputum smears or M. tuberculosis on culture of sputum or gastric washings and a positive tuberculin reaction. The symptoms have a fairly reliable pattern, but together with the physical signs are unreliable in the diagnosis and differential diagnosis except in the late stages of the disease.

2. The treatment of pulmonary tuberculosis may conveniently be divided into five parts: (1) chemotherapy, (2) rest and education, (3) collapse, both temporary and permanent, (4) pulmonary resection, and (5) other measures.

Current Status of Antimicrobial Agents in the Treatment of Pulmonary Tuberculosis

NICHOLAS D. D'ESOPO, M.D., *West Haven, Connecticut*

A GREAT deal has been learned about antituberculosis drugs during the past eight years; yet many questions remain unanswered relating to drug regimens and to the influence of chemotherapy in general upon the indications for thoracoplasty, resection and bed rest. Diverse clinical practices appear to give equally satisfactory results. In fact, few applications of chemotherapy can be carried out with a deep conviction that they are the best. Many clinical studies are incomplete. It seems best, therefore, to discuss the present status of chemotherapy of pulmonary tuberculosis simply as an interpretation of the clinical and laboratory data upon which current clinical practices now rest.

CHANGES IN THE MORPHOLOGY OF TUBERCULOUS LESIONS

The antituberculosis drugs we now have are chiefly bacteriostatic and their therapeutic effect results from the suppression of tubercle bacilli in the tuberculous lesion. Morphologic changes in the lesions are not qualitatively different* from those which occur in the natural course of the disease or with bed rest and collapse therapy. Morphologic changes can be described as if they occurred in three different types: (1) the non-necrotic lesion, (2) the solid necrotic lesion, and (3) the necrotic lesion which has liquefied and sloughed to form a cavity. This is an over simplification which the clinician may find useful as he follows the evolution of lesions on serial x-rays during chemotherapy.

The non-necrotic lesion comprises both the non-necrotic tuberculous lobular pneumonia *per se* and the so-called non-specific "perifocal reaction." The term "tuberculous lobular pneumonia" is reserved for the inflammatory process due to the tubercle bacillus itself; the term "perifocal reaction" has been given to the collections of cells which are presumably a non-specific response to tuberculoprotein in a hypersensitive host. Emphasis is placed upon the non-necrotic character of both types of exudates quite apart from their pathogenesis. In both processes the inflammatory cells are viable and there has been no death of lung tissue. The earliest change noted by x-ray after the institution of chemotherapy is believed to be the resolution of non-necrotic lesions. This is represented by the rapid clearing of x-ray shadows during the first several months of chemotherapy. Clinical observation suggests that resolution of non-necrotic lesions occurs more promptly and more rapidly with chemotherapy than with any other therapy. However, the contribution of chemotherapy is neither the rate nor extent of resolution; rather it is that resolution is predictable and progressive.

The second type is the solid necrotic lesion. In this lesion the cells of the exudate and parenchyma of the lung are dead but the process has not progressed to autolysis and liquefaction. The lesion is a coagulated mass of necrotic material which becomes surrounded by a capsule of fibrous tissue. The tuberculoma is a large necrotic lesion of this type. Solid necrotic lesions are influenced to a minimal extent if at all by chemotherapy. However, they are commonly mixed lesions. Having sloughed in part, they may contain a small cavity; they are also frequently closely surrounded by small non-necrotic lesions. Favorable changes in these subsidiary elements are reflected on the x-ray by a decrease in size of the total lesion and a sharper definition of its borders.

The third variety is the necrotic lesion which has progressed to liquefaction and sloughing to form an air-containing cavity. Its response to chemotherapy is a reduction in size and, under the best circumstances, complete closure.

* Some pathologists believe that the non-specific inflammation occurs to a lesser extent during chemotherapy, resulting in a particularly thin capsule around necrotic lesions and fewer pleural adhesions.

The closure of cavities is in reality a process of their filling-in with inspissated necrotic material. This occurs not only when cavities close under the influence of drugs, but also in the natural course of the disease and with other forms of therapy. Only in exceptional instances does the necrotic inner wall of the cavity slough out completely so that uninfected granulating surfaces organize into a scar. Filled-in or closed cavities therefore are not healed in a morphologic sense. Much is gained when an open necrotic lesion is made airless since this is an environment in which tubercle bacilli do not freely multiply. However, as Medlar has shown so well, detailed examination of the resected filled-in cavity often reveals one or more bronchioles traceable into its interior. These bronchioles, containing necrotic debris, pierce the fibrous connective tissue wall of the filled-in cavity. The risk is that they can become the pathway to relapse if the material in the filled-in cavity should liquefy and empty. Whether or not the viability of the bacilli in the closed necrotic lesion has been modified during chemotherapy will be discussed presently.

Cavity closure does not always follow successful bacterial suppression by potent antituberculosis agents. Sputum cultures may be negative for months and yet cavities may remain open. Rarely does the necrotic inner wall of such open cavities slough out completely, resulting in a cyst-like structure lined with either connective tissue or bronchial epithelium. In the majority, necrotic portions of the cavity wall remain in which tubercle bacilli are found. Such open cavities are often thin-walled and resemble emphysematous bullae which so often occur in lungs that have been heavily involved. The two structures cannot be distinguished by x-ray.

In summary, it may be said that after maximal resolution of lesions has occurred and all cavities have closed, the lesions that remain are necrotic. They are either solid, unsloughed lesions which changed little or not at all during chemotherapy, or they are filled-in cavities. Roentgenographically, it is not possible to differentiate the two types; both may cast sharply defined and even linear shadows. While there is considerable doubt about the best therapy of the residual necrotic lesions after chemotherapy, there is no question about their morphology. It may be added that cavities which do not close during chemotherapy are open necrotic lesions which very probably harbor viable tubercle bacilli even though the sputum cultures may be negative.

BACTERIOLOGY OF TUBERCULOUS LESIONS UNDER CHEMOTHERAPY

During the past several years the viability* of tubercle bacilli in resected lesions has received considerable attention. It has long been known that tubercle bacilli may not survive in tuberculous lesions during the natural course of the disease.[1–4] Recently it has been possible to study bacilli in lesions resected at operation, usually after chemotherapy. The bacteriology of these lesions can be satisfactorily interpreted only when the clinical conditions under which the resections were carried out are clearly set forth. The factors which have the most bearing on the viability of bacilli are: whether the chemotherapeutic regimen is an original or retreatment course; whether streptomycin is administered daily or twice weekly; the duration of preoperative chemotherapy; the bacteriology of the sputum during the two to three-month interval preceding resection; and, finally, the morphology of the resected lesion, whether it is open (i.e., an air-containing cavity) or closed.

The bacteriology of resected lesions in a series reported from Sunmount Veterans Administration Hospital was studied in lesions resected after a definite clinical "therapeutic target point" had been reached.[5] This point is defined as the time when (1) all the cavities have closed, (2) the sputum or gastric cultures are consistently negative,† and (3) maximum resolution of lesions on roentgenograms has occurred. In the patients who received streptomycin 1.0 gm. every day and PAS 12.0 gm. daily only 5.2 per cent of resections yielded lesions from which viable bacilli were demonstrated by culture or animal inoculation. In patients treated with streptomycin 0.5 gm. daily and PAS 12.0 gm. daily the incidence of lesions with viable bacilli was 17 per cent, while in those treated with streptomycin 1.0 gm. twice weekly and PAS 12.0 gm. daily the incidence was 35 per cent. The majority

* Throughout this article "viability of tubercle bacilli" means the capacity to multiply on artificial culture media or to cause infection in susceptible animals. It is recognized that bacteria may do neither and yet be alive.

† Usually this means three months. In extensive lesions a longer period of negative cultures was required.

of the lesions (approximately 70 per cent) harbored bacilli visible on smear or stained sections. These data have been confirmed by other investigators. In a series of 125 patients reported by Steele[6] 8 per cent of resections yielded lesions with viable bacilli. In the series of Falk et al.[7] (which included both original and retreatment cases) 12 per cent of resected cases had viable bacilli. The lesion in which non-viable bacilli are found may be either a filled-in cavity or a solid necrotic lesion which had never sloughed. The size of the filled-in cavity does not seem significant. Large filled-in cavities often contain myriads of bacilli on stained smear which are not viable by animal inoculation or culture. On the other hand, viable bacilli can be recovered from the majority of resected open cavities (air-containing cavities) even after very prolonged courses of chemotherapy.

There is no agreement among bacteriologists that these bacilli in closed necrotic lesions are really dead. It is suggested that chemotherapeutic agents or substances in closed necrotic lesions may have modified the growth characteristics of bacilli in such a way that standard culture methods may be inadequate to test their viability. Dubos[8] has called attention to certain products of tissue necrosis in tuberculous lesions, i.e., fatty acids, spermine and lactic acid, which are strongly tuberculostatic and even tuberculocidal. Such inhibitory substances may be adsorbed upon the bacilli preventing their multiplication. Recently Hobby[9] has investigated this aspect of the problem with a bovine albumin technic to neutralize components of necrotic lesions. This method has yielded viable bacilli from closed necrotic lesions in eleven of fifteen patients—an incidence of 73 per cent. The albumin technic was not controlled by standard media. Without controls it is impossible to assess the significance of certain factors of the clinical material from which the lesions were obtained. Most of the patients in Hobby's series received streptomycin twice weekly preoperatively; the duration of chemotherapy was on the average less than eight months; and some received retreatment courses of chemotherapy. These factors may account in large part for the high incidence of viable bacilli. In the Sunmount study, for example, patients who received twice weekly streptomycin and daily PAS and came to resection after from four to eight months of chemotherapy had an incidence of viable bacilli of 50 per cent as compared to 8 per cent* in those treated with daily SM and PAS for the same length of time. The difference in the incidence of viable bacilli in the two groups emphasizes the necessity of controlling new culture methods by standard technics in order to take into account factors such as regimen and duration of chemotherapy.

If bacilli in closed necrotic lesions are dead, is this a primary effect of chemotherapy? There are several observations which suggest that this is improbable. Before the era of chemotherapy it had been shown that bacilli in many tuberculous lesions could not be cultured.[1–4] Solid necrotic lesions which are now sometimes resected without preoperative chemotherapy often have non-viable bacilli within them. On the other hand, viable bacilli can be demonstrated in open cavities even after very long courses of chemotherapy. It is evident, therefore, that bacilli may die in necrotic lesions never exposed to antituberculosis drugs; on the contrary, bacilli in open lesions exposed to very long periods of chemotherapy are usually viable. It seems clear that it is the morphology of necrotic lesions, not chemotherapy, which is the factor most closely related to the death of bacilli, if indeed they are dead.

Does the finding of non-viable bacilli in closed necrotic lesions have practical clinical applications? Recovery from tuberculosis under natural conditions depends chiefly upon the closure of open necrotic lesions. We have seen that prolonged chemotherapy can bring about this morphologic change. In the writer's opinion, the principle contribution of the data on the viability of bacilli in closed necrotic lesions is to encourage clinical studies to explore the value of chemotherapy as definitive therapy. The clinical significance of these laboratory data will be learned not by devising new methods of testing the viability of bacilli, but rather by the fate of those patients whose closed necrotic lesions were not resected after treat-

* In the reference[5] quoted above, eighteen resections in the streptomycin 1.0 gm. daily–PAS 12.0 gm. daily group performed between the fourth and eighth months of treatment yielded one positive lesion. Unpublished additional data bring this group to two positive lesions of twenty-four resections (8 per cent). In the article quoted, six resections in the streptomycin 1.0 gm. twice weekly–PAS 12.0 gm. daily group yielded three positive lesions; additional data bring these to five positive lesions of ten resections, the incidence of positive lesions remaining the same (50 per cent).

ment with prolonged chemotherapy. In the meantime these data are bound to influence the indications for the resection of closed necrotic lesions—a point to be discussed later in this article.

DRUG RESISTANCE

Drug resistance* is the most important cause for the failure of combined chemotherapy after we exclude from consideration patients with extensive destruction of lung tissue. Failure of chemotherapy usually means failure of cavity closure. With our present drugs the sustained bacterial inhibition necessary to achieve cavity closure can be attained only by the preservation of bacterial sensitivity.

Data from a Medical Council Research Study indicate that INH is at least as effective as PAS in preserving the sensitivity of bacilli to streptomycin.[11] In patients treated with SM-INH only 8 per cent of positive cultures were resistant to SM at the end of three months and 0 per cent at the end of six months of therapy.

On the other hand, streptomycin is effective in preserving sensitivity to INH. In patients treated with SM-INH the incidence of INH-resistance at the end of three and six months was 11 and 50 per cent, respectively. These results suggest that INH may be more effective in preserving bacterial sensitivity to streptomycin than is streptomycin in preserving sensitivity to INH. However, in the Medical Research Council study, streptomycin was administered daily for only the first three months; after that, the SM dosage was usually reduced to 1.0 gm. twice weekly. It would not be surprising to learn that streptomycin is less effective in preserving INH sensitivity when it is administered twice weekly rather than daily. The effectiveness of streptomycin in preserving INH sensitivity has also been demonstrated in the cooperative study of the Veterans Administration, Army and Navy.[12] These data also indicate that PAS maintains sensitivity of bacilli to INH as well as it does to streptomycin.

Combined chemotherapy effectively reduces the chances of bacterial resistance but the threat of resistance is always present. Two general principles may be followed to prevent or delay it. The first is the continuous and uninterrupted administration of combined drugs. The second is the closure or resection of cavities which have not closed during the first four to six months of treatment. There is a strong association between bacterial resistance and the presence of open cavities. During chemotherapy sputum cultures may remain negative for months in the presence of large open cavities. However, as long as cavities remain open, bacteriologic relapse and resistance may occur even if chemotherapy is continued uninterruptedly. Every effort, therefore, should be made to close or resect large cavities. In combined SM-PAS therapy, procedures to this end need not be undertaken before the fourth to fifth month except when cavities are very large. With small open cavities (2 cm. or less) the risk of bacterial relapse and resistance is slight. It may be pointed out that when bacteriologic relapse occurs, resistance is more frequent with the daily SM-PAS regimen than with twice weekly SM-daily PAS. The relationships between open cavities, bacteriologic relapse and resistance during therapy with INH regimens have not yet been sufficiently clarified. In the meantime, it seems best to assume that in these regimens, also, the open cavity invites bacterial relapse and resistance.

VIRULENCE OF BACILLI EXPOSED TO ANTIMICROBIAL AGENTS

In experimental animals bacilli resistant to streptomycin have the same degree of virulence as the parent strains, and clinical experience bears this out. Bacilli resistant to INH, however, are often avirulent for animals.[13,14] Virulence appears to vary with different species: mice are susceptible to INH-resistant organisms; guinea pigs are usually not. The avirulence of INH-resistant strains is related in only a general way to the degree of INH resistance. Most of the avirulent strains are highly resistant to INH, but a few are INH-sensitive. On the other hand, some highly resistant strains are quite virulent for guinea pigs.[14] These apparent inconsistencies may be due to a mixed bacterial population. It is believed by some that the sensitive strains in a population which is predominantly resistant may account for its virulence.

* Bacilli capable of growth in 10 μg. of streptomycin per ml. of media are considered to have a degree of resistance which is clinically significant. The corresponding values for PAS and INH® are 10 and 1 μg. per ml. of media, respectively. The value for INH is uncertain; but when infection can be established in guinea pigs by strains resistant to 1 μg. of INH, doses of INH comparable to those used in man do not protect the animals.[10]

The virulence of INH-resistant strains may be inconstant. Certain avirulent cultures become virulent in time. If the explanation in the preceding paragraph is correct, this may be due to a relative increase in the proportion of sensitive bacilli in the total bacterial population.

Does the phenomenon of avirulence of INH-resistant strains have any bearing on the treatment of human tuberculosis? Several clinical observations indicate that the emergence of INH-resistant strains is detrimental to the patient under therapy. The appearance of INH-resistant bacilli in man is frequently. though not always, attended by an increase in the number of bacilli being discharged in the sputum. Worsening of the disease during INH therapy as revealed by x-ray changes or clinically is usually associated with the emergence of INH-resistant bacilli *in vitro*. Furthermore, there is no direct relationship between the clinical course of the patient and the virulence of organisms for laboratory animals: lesions can progress while INH-resistant bacilli recovered in the sputum may be non-pathogenic for guinea pigs.[14,15] Finally, when the patient with bacilli resistant to INH is treated with streptomycin combined with INH, INH fails to prevent SM-resistance: bacilli become resistant to streptomycin just as if streptomycin alone were used. One cannot escape the conclusion that the emergence of INH-resistant strains is disadvantageous to the patient, and everything should be done to prevent their occurrence.

EFFICACY OF CHEMOTHERAPY REGIMENS

Studies of the therapeutic efficacy of several drug regimens are now in progress. In a study being conducted by the U. S. Public Health Service a comparison of the regimens, INH-SM and INH-PAS, suggests that there is no superiority of one over the others.[16] Moreover, three drugs given simultaneously have shown no advantage over combinations of only two drugs. Two dosages of INH, 3 and 10 mg/kg., showed no significant therapeutic differences, but the larger dose caused appreciably greater toxicity. In this study SM-INH had a slight but consistent superiority over SM-PAS.[17] At the end of the forty weeks of therapy 68 per cent of patients treated with SM-PAS had negative cultures as compared to 82 per cent in the SM-INH group. X-ray improvement was slightly greater in the SM-INH treated patients, 78 per cent as compared to 71 per cent in the SM-PAS group.

In a preliminary evaluation by the Veterans Administration, Army and Navy Study Units,[18] the therapeutic efficacy of all three regimens, INH-PAS, INH-SM and SM-PAS, showed no significant differences. At the eighth month of therapy sputum conversion had occurred in 70 per cent of patients in the three regimens. X-ray improvement was also similar—approximately 50 to 60 per cent.

It is emphasized that studies of the comparative efficacy of combined drug regimens are incomplete. Moreover, the data obtained thus far assess the regimens chiefly in terms of x-ray changes and sputum conversion. We must still await a definitive evaluation in terms of the incidence of cavity closure and relapse. In the meantime no one regimen appears to be significantly superior to the others.

In the light of these data the choice of a regimen for the individual patient is a decision which may depend chiefly upon the risks of bacterial resistance, once having excluded from consideration toxicity and hypersensitivity manifestations. On theoretic grounds it would seem best to avoid using the two major drugs, SM and INH, in the initial course of treatment but to select, rather, a regimen of one major and one minor drug. Of the two combinations of a major and minor drug, there is some justification for choosing SM-PAS instead of INH-PAS. If bacterial resistance should occur, INH could be available when the need for retreatment arises. In single drug therapy INH may be superior to SM for at least two reasons: its greater efficacy in miliary and meningeal tuberculosis, and the fact that resistance to INH may not be as disadvantageous as resistance to SM.

When cases are retreated, the regimens to be employed depend upon the sensitivity of bacilli to drugs previously used. Here the physician must have *in vitro* sensitivity tests to all drugs, including PAS, in order to prescribe the best retreatment regimen. When bacilli are resistant to PAS, the retreatment regimen of choice is certainly SM-INH. However, the combination of oxytetracycline (terramycin®) 1 to 2 gm. daily and SM 1.0 gm. twice weekly may be used. This should not be understood as suggesting that TM with SM

is as effective as INH with SM; rather, that TM has the action of PAS in preventing SM resistance. It is not known whether terramycin delays resistance to streptomycin to a clinically significant degree when streptomycin is administered daily.

When bacilli are resistant to both SM and PAS, INH may be paired with either pyrazinamide or oxytetracycline. However, the efficacy of these regimens is not yet established. The combination of PZA-INH is effective in experimental animals,[19] and preliminary results suggest that it may be useful in man.[20] PZA, however, is a hepatotoxic drug and at this writing is not yet available for routine use. Data on the regimen of INH-TM are incomplete but TM appears to be partially successful in maintaining sensitivity to INH.[21]

Patients whose organisms are resistant to both SM and INH may be treated with viomycin 2.0 gm. twice weekly combined with PAS, 12 gm. daily. Viomycin is not a particularly effective drug but it is always worth a trial.[22]

When bacilli exhibit a moderate rather than a high degree of resistance to drugs, the selection of the proper drugs may be difficult. In general it is best to avoid using a drug to which bacilli are moderately resistant because of the risk of later developing resistance to the drug with which it is paired. Moderate resistance may be defined, in the case of streptomycin, as growth of bacilli in 10 but not in 100 μg. per ml.; for PAS, as growth in 10 but not in 100 μg. per ml.; and for INH, as growth in 1.0 but not in 5.0 μg. per ml.

Multiple drug therapy dates from 1948 and has been advocated in the chemotherapy of tuberculosis ever since. Indeed, it has been considered improper to prescribe single drugs except in unusual circumstances. Recent experience with isoniazid, however, seems to have cast doubt upon this concept. In the U. S. Public Health Study isoniazid alone was as effective as either SM-INH or PAS-INH in non-cavitary disease.[23] Deuschle et al.[24] recently described an encouraging experience with a group of patients treated with isoniazid alone for one year. Such clinical trials should be encouraged not only because of the practical advantages of single drug therapy but also because they challenge what has been regarded a fundamental principle of chemotherapy. However, until more is learned about the late results of single drug therapy, combined chemotherapy should be considered obligatory in clinical practice.

OPTIMUM DURATION OF CHEMOTHERAPY

The optimum duration of chemotherapy in the treatment of pulmonary tuberculosis is not known. From 1946 to 1948, when streptomycin was our only antituberculosis drug, duration was limited chiefly by bacterial resistance. Tubercle bacilli usually became highly resistant by the third month of therapy, after which there was little if any advantage in continuing. Now the duration of chemotherapy may be indefinitely prolonged because combined drugs tend to prevent bacterial resistance.

The problem of the optimum duration of chemotherapy may be considered in patients in three radiographic-bacteriologic phases: (1) when all cavities have closed and sputum cultures have become negative, (2) when cavities have remained open but the sputum has been negative, and (3) when the patient's cavities have remained open and the sputum is positive. When maximal resolution of lesions has occurred, patients in the first phase have attained the therapeutic target point previously described and thus appear to be in a particularly favorable condition. How much more chemotherapy is required is not known. Realizing the disadvantage of stopping drugs prematurely, many physicians are now inclined to advise chemotherapy for very long periods of time. Undoubtedly the amount and character of disease, the patient's previous experience with tuberculosis, the history of relapse and various socio-economic conditions such as the necessity to return to work are factors taken into account. Patients with minimal lesions are often treated for one year or more even though the initial lesion may have been extremely small. Currently the optimum duration of drugs is the subject of a control study by hospitals in the Veterans Administration, Army and Navy Study. In this study once the target point is reached additional chemotherapy depends upon random selection, alternate patients being treated for either six or twelve months. This study is not complete since it is obvious that its assessment must be in terms of relapse rates. Until more precise data are at hand, it is believed that chemotherapy should be continued in

this group of patients for at least six months beyond clinical goals more or less comparable to the "therapeutic target point."

The problem of the duration of chemotherapy is more complex in the second phase, i.e., in the patients whose cavities remain open but whose sputum cultures are negative. It has been pointed out that because of the risks of bacterial relapse and resistance every effort should be made to collapse or resect open cavities. Often, however, no procedure can be performed to close cavities. There are no reliable guides to the duration of chemotherapy in such patients. Some physicians believe that drugs should be continued indefinitely. As long as cavities remain unclosed, there is always the risk of relapse, either during chemotherapy or after its termination.

The writer does not wish to imply that the two phases just described can always be distinguished. It is often impossible to rule out the presence of open cavity. This is an especially difficult decision in confluent lesions located high in the apex of the lung. It is impossible in many instances to differentiate between open cavities and emphysematous bullae. Such patients should be treated as if an open cavity were present: Collapse or resection should be performed whenever possible; the alternative is the continuation of drugs.

In the third phase patients fail to achieve both closure of all cavities and sputum conversion. When cavity closure and sputum conversion have not occurred by the sixth and certainly the eighth month of uninterrupted original chemotherapy, it is improbable that they will occur by the continuation of the same drugs. Other drugs or other therapeutic procedures, such as surgery, will be found necessary. When neither of these alternatives is feasible, the current course of chemotherapy should be continued and terminated only when it is judged to be no longer beneficial to the patient. The chief guides here are unequivocal clinical deterioration or progressive worsening of disease by x-ray. The sensitivity of the organisms *in vitro* is not a reliable criterion.

SURGERY AND CHEMOTHERAPY

In practice the relationships between surgery and chemotherapy are approached from two diverse points of view. In one, surgery is performed as early as possible, chemotherapy being employed in a secondary role. In the other view, surgery is performed either late in the course of chemotherapy or not at all if drugs have been particularly effective. When chemotherapy is used as primary therapy, each case of pulmonary tuberculosis falls at one time or another into the three phases in which the duration of chemotherapy was discussed: (1) All cavities are closed and sputum cultures are negative; (2) there are one or more open lesions but sputum cultures are negative; (3) there are open lesions and sputum cultures are positive. As a *primary* therapy chemotherapy is successful in the first pattern only; in the remaining two it has failed. The majority of minimal or moderately advanced cases (NTA 1950) treated with original uninterrupted chemotherapy will attain the first phase: closed lesions and negative sputum.* A number of the more favorable far advanced cases will also reach this status. After maximal resolution of lesions the residual lesions are either solid unsloughed necrotic lesions or filled-in cavities. Early in 1950 the morphologic characteristics of residual necrotic lesions, specifically the potential bronchial communications of filled-in cavities, stimulated a clinical study in which all residual necrotic lesions were resected. This study[26] and others[27,28] which followed demonstrated that residual necrotic lesions can be resected with almost no tuberculous complications and very little morbidity in general. Data upon the non-viability of bacilli in closed necrotic lesions, however, have raised some doubt about the necessity for resecting them. It is to be expected that in practice the use of surgery in the treatment of these lesions is influenced by the interpretation of these bacteriologic data: If the bacilli in residual necrotic lesions are dead, there is no need for resection; if, on the other hand, bacilli are not dead, the morphologic features of the lesions might possibly warrant resection. We must conclude that at the present time we do not know the clinical significance of either the morphology or bacteriology of these lesions. A three-year follow-up of resected and non-resected residual necrotic lesions which attained the target point under prolonged chemotherapy has shown no differences in relapse

* This is true of daily SM-PAS; experience with INH regimens is too recent.

rate thus far.[29] More data of this kind are necessary. A control study on the indications for resection of closed necrotic lesions is in progress in several Veterans Administration, Army and Navy Hospitals.

A considerable number of patients fall into the second clinical pattern: open cavities and negative sputum culture. This phase is often temporary since in many instances the sputum becomes positive again. The integration of resection or thoracoplasty with chemotherapy is therefore of great importance. The probability of cavity closure on drugs alone* may be assessed; and whenever it seems unlikely, surgery should be performed while the sputum is still negative. The tuberculous complications of resection are minimal in this phase.

In the third phase are the patients whose cavities have not closed and sputum has remained positive during chemotherapy. Usually these cavities are large; many patients have been treated before and organisms are resistant to major antituberculosis drugs. These cases are failures of chemotherapy and their management is often no different from that in the prechemotherapy era. Occasionally it is possible to add other drugs which may diminish the risks of surgical complications. In general, thoracoplasty rather than resection will be preferred if surgery can be performed.

When surgery is employed as primary therapy, it is undertaken as soon as the patient's general condition has improved and the number of bacilli in the sputum has diminished. In this approach surgery is performed *before* maximum resolution of lesions has occurred under the influence of chemotherapy. Advanced lesions in which chemotherapy is bound to fail are often treated in this way. Early surgery is advocated too, because bacterial resistance is apt to occur rapidly in advanced lesions.

Small localized lesions also are resected after a brief period of chemotherapy which is employed here in a prophylactic role. The rationale of this practice is that the resolution of non-necrotic lesions during a long course of chemotherapy may not result in a less extensive surgical procedure; or that a wedge resection is no more advantageous than a segmental resection, or that complications will be no greater and no saving of lung tissue will result if surgery is performed later. No doubt these are valid assumptions in many cases, and it has been amply demonstrated that early surgery can be carried out with few complications.

There is no reason to advocate one or the other of these two fundamental therapeutic points of view. We do not know enough about the interrelations of surgery and chemotherapy to do so. In practice, the therapeutic problems presented by the individual case will usually incline the medical-surgical team toward one or the other approach. However, the two therapeutic points of view, in the writer's opinion, have a bearing upon the investigation of the indications for surgery during chemotherapy. In the far advanced, especially the very far advanced, cases chemotherapy as primary therapy fails so often that surgical procedures may be planned almost from the very start of chemotherapy. What we need to investigate here is the proper timing of surgery, especially how long surgical procedures may be delayed without running the risks of bacterial resistance.

In minimal and moderately advanced cases, however, these alternate therapeutic points of view will have a decided effect upon the development of surgical indications. Most minimal and moderately advanced cases treated with original chemotherapy can be brought to the phase of closed necrotic lesions with consistently negative sputum. The policy of early surgery, with chemotherapy in a prophylactic role, does not foster the investigation of chemotherapy as a definitive therapy in these cases. It is entirely possible that resection is not necessary to prevent relapse of these lesions. The early resection of small or moderate-sized lesions is often advocated as a saving of time and hospitalization. This may be an advantage at present. However, if ambulatory chemotherapy and home chemotherapy have the success they promise, the objection of long hospitalization and loss of time from work will largely pass.

In the literature it is often impossible to recognize the relationships between surgical

* Closure of cavity is related chiefly to size and location. The incidence of closure of cavities 6 cm. or less is very high during the first five to six months of original uninterrupted chemotherapy. Cavities of larger size, i.e., 10 cm. in diameter, can only rarely be expected to close on chemotherapy. Cavities high in the apex of the lung, those in contracted lobes and those in the midst of dense necrotic disease have less tendency to close under chemotherapy (or any other therapy).

procedures and chemotherapy because factors which are known or presumed to be related to tuberculous complications and relapse are not documented. The most important are: whether the course of chemotherapy used was original or retreatment; whether, if a retreatment course, organisms were sensitive or resistant; whether chemotherapy was continuous or interrupted; the duration of preoperative chemotherapy; whether sputum cultures were positive or negative during the several months preceding operation; whether open cavity or cavities were present preoperatively; whether maximal resolution of lesions had occurred prior to operation; the size of the residual necrotic lesions which were resected; the duration of chemotherapy postoperatively; and the bacteriology and morphology of the resected lesions. A better description of the disease at the time chemotherapy was begun would also be instructive, especially the number of cavities, the size of the largest cavity and whether the cavities were unilateral or bilateral. Often relatively little can be learned from the data recorded except a very general idea of operability, mortality and complications.

SUMMARY

In the treatment of pulmonary tuberculosis three combinations of antituberculosis drugs, SM-PAS, SM-INH and INH-PAS, appear equally effective. Differences between them, however, may be evident upon completion of studies now in progress. If these regimens were equally effective, the selection of SM-PAS for initial therapy would leave INH, the more versatile of the two major drugs, in reserve for retreatment if it should become necessary. Drug resistance is effectively delayed by all three combinations of drugs, but the particular advantages, if any, of one combination over another in this respect have not yet been clarified. Toxicity of drugs is now a relatively unimportant consideration either in the selection of a regimen or in the duration of chemotherapy.

Whatever regimen is employed, there is now general agreement that uninterrupted drug therapy should be continued for at least one year, or six to twelve months after a target point of (1) closure of all cavities, (2) persistently negative sputum cultures and (3) maximal resolution of lesions, has been achieved. However, the optimum duration of chemotherapy is not known.

The changes in the morphology of tuberculous lesions following the use of drugs do not differ qualitatively from those occurring with other forms of therapy. However, resolution is prompt and predictable. Solid necrotic lesions are affected relatively little. Cavity closure is usually a process of their filling in with necrotic material, and potential bronchial communications can often be demonstrated between the filled-in cavity and the bronchial tree. Filled-in cavities are not healed in a morphologic sense and thus there may be a rationale for resecting them. Yet bacilli are non-viable in closed necrotic lesions in 85 to 95 per cent of resections. There is no general agreement, however, that such bacilli are in fact dead. In the meantime the interpretation of these bacteriologic data is bound to influence the indications for resection of closed necrotic lesions. The relationships between surgery and chemotherapy not only involve the interpretation of the morphology and bacteriology of closed necrotic lesions, but depend also upon whether the primary role in the treatment of pulmonary tuberculosis is given to chemotherapy or to surgery.

REFERENCES

1. Sweany, H. C. Age Morphology of Primary Tubercles. Springfield, Ill., 1941. Charles C Thomas, Publisher.
2. Sweany, H. C. Age characteristics of tubercles. *Am. Rev. Tuberc.*, 46: 329, 1942.
3. Sweany, H. C., Levinson, S. A. and Stadnichenko, A. M. S. Tuberculous infection in people dying of causes other than tuberculosis. Ibid. 48: 131, 1943.
4. Canetti, G. Le bacille de Koch dans la lésion tuberculeuse du Poumon. France, 1946. Editions Médicales Flammarion.
5. D'Esopo, N. D., Bernsetin, S., Decker, A. M., Raleigh, J. W. and Steenken, W., Jr. Bacteriology of lesions resected during chemotherapy. Transactions of the Twelfth Conference on the Chemotherapy of Tuberculosis, Veterans Administration, Washington, D.C., February, 1953.
6. Steele, J. D. The bacteriology of resected tuberculous pulmonary lesions. Ibid.
7. Falk, A., Kaufman, J. E. and Tucker, W. B. Resectional surgery in pulmonary tuberculosis with a bacteriologic study of the resected tissue. Ibid.
8. Dubos, R. J. Viability of tubercle bacilli in vitro with and without chemotherapy. *Am. Rev. Tuberc.*, 67: 874, 1953.
9. Hobby, G. L., Auerbach, O., Lenert, T. F., Small, M. J. and Comer, J. V. The late emergence of M. tuberculosis in liquid cultures of pulmonary lesions resected from humans. *Am. Rev. Tuberc.*, 70: 191, 1954.

10. Mitchison, D. A. Tubercle bacilli resistant to isoniazid; virulence and response to treatment with isoniazid in guinea-pigs. *Brit. M. J.*, 4854: 128, 1954.
11. Medical Research Council Report. Emergence of bacterial resistance in pulmonary tuberculosis under treatment with isoniazid, streptomycin plus P.A.S. and streptomycin plus isoniazid. *Lancet*, 2: 217, 1953.
12. Transactions of the Thirteenth Conference on the Chemotherapy of Tuberculosis, Veterans Administration, Washington, D.C., February, 1954.
13. Barnett, M., Bushby, S. R. M. and Mitchison, D. A. Isoniazid-resistant strains of tubercle bacilli; their development and stability. *Lancet*, 1: 314, 1953.
14. Steenken, W., Jr. and Wolinsky, E. Virulence of tubercle bacilli recovered from patients treated with isoniazid. *Am. Rev. Tuberc.*, 68: 548, 1953.
15. Panel Discussion: Relationship between the emergence of resistance to INH by tubercle bacilli and their pathogenicity for experimental animals and (as estimated by relapse) for man. Transactions of the Twelfth Conference on the Chemotherapy of Tuberculosis, Veterans Administration, Washington, D.C., February, 1953.
16. Progress report on therapeutic and toxic effects of combinations of isoniazid, streptomycin, and para-ammosalicylic acid. United States Public Health Service Cooperative Investigation of Antimicrobial Therapy of Tuberculosis. *Am. Rev. Tuberc.*, 69: 1, 1954.
17. Mount, F. W., Jenkins, B. E. and Ferebee, S. H. Control study of comparative efficacy of isoniazid, streptomycin-isoniazid, and streptomycin-para-aminosalicylic acid in pulmonary tuberculosis therapy. *Am. Rev. Tuberc.*, 68: 264, 1953.
18. Transactions of the Thirteenth Conference on the Chemotherapy of Tuberculosis, Veterans Administration, Washington, D.C., February, 1954.
19. McCune, R. and Tompsett, R. Effect of pyrazinamide—isoniazid and other anti-tuberculous drugs on populations of M. tuberculosis in experimental animals. Ibid.
20. Moyer, R. E. Results of long term chemotherapy with pyrazinamide and isoniazid on human tuberculosis. Transactions of Thirteenth Conference on the Chemotherapy of Tuberculosis, Veterans Administration, Washington, D.C., February, 1954.
21. Unpublished data.
22. Hobby, G. Viomycin: Summary of a four-year evaluation. Transactions of Twelfth Conference on the Chemotherapy of Tuberculosis, Veterans Administration, Washington, D.C., February, 1953.
23. Eckley, G. Evidence suggesting differential effects of various drug regimens in pulmonary tuberculosis. Transactions of Thirteenth Conference on Chemotherapy of Tuberculosis, Veterans Administration, Washington, D.C., February, 1954.
24. Deuschle, K., Ormand, L., Elmendorf, D., Jr., Muschenheim, C. and McDermott, W. The course of pulmonary tuberculosis during long-term single drug (isoniazid) therapy. *Am. Rev. Tuberc.*, 70: 228, 1954.
25. Biehl, J. P. and Vilter, R. W. Effects of isoniazid on pyridoxine metabolism. Transactions of Thirteenth Conference on Chemotherapy of Tuberculosis, Veterans Administration, Washington, D.C., February, 1954.
26. Ryan, B. J., Medlar, E. M. and Welles, E. S. Simple excision in the treatment of pulmonary tuberculosis. *J. Thoracic Surg.*, 23: 327, 1952.
27. Steele, J. D., Narodick, B. G. and Cadden, A. V. The influence of long-term chemotherapy on the surgery of pulmonary tuberculosis. *J. Thoracic Surg.*, 26: 459, 1953.
28. Murphy, J. D. A study of the factors influencing the success of segmental resection for pulmonary tuberculosis. Transactions of Thirteenth Conference on the Chemotherapy of Tuberculosis, Veterans Administration, Washington, D.C., February, 1954.
29. Raleigh, J. W., D'Esopo, N. D., Osgood, C. K. and Campbell, A. M. Relapse following streptomycin-para-aminosalicylic acid therapy for pulmonary tuberculosis. Ibid.

Pathology of Tuberculosis As Affected by Antibiotics

OSCAR AUERBACH, M.D., *East Orange, New Jersey*

From the Laboratory Service, Veterans Administration Hospital, East Orange, N. J. Read in part at the Primeras Jornadas Medicas, Instituto Nacional de Neumologia, Mexico City, Mexico, June 13–19, 1954.

CHANGES in pulmonary tuberculosis brought about by chemotherapy are striking and consistent. It is of interest also that the changes are similar no matter what combination of drugs is used, as long as tubercle bacilli remain sensitive to the drugs. This would speak for the fact that the drugs neutralize the action of the organisms and healing changes become the dominant feature of the tuberculous process.

In the usual course of events, when no chemotherapy is employed, pulmonary tuberculosis is characterized by progression of the disease with concomitant repair. The natural evolution of the tuberculous process is the development of a cavity in the upper lobe. In a small percentage of instances this may close without the aid of collapse therapy. Generally, the cavity enlarges and, with the dissemination of tubercle bacilli to other parts of the lung, new areas of tuberculous pneumonia develop which may either liquefy and form cavities or may become walled-off by the elements of repair. The spread of the disease to other parts of the lungs would continue until pulmonary insufficiency resulting from extensive disease would terminate the patient's life. It is of interest that the duration of the disease in these individuals was less than two years in the great majority of instances. More than 80 per cent of this group showed intestinal tuberculosis and more than 40 per cent had laryngeal tuberculosis. It is in this group of patients that collapse therapy was frequently employed in an attempt to close the cavities. Generally, the procedures were applied when the cavities were still limited to the upper lobe and before extensive spread of the disease had occurred. Success was dependent upon closing the communication between the cavities and the draining bronchi.

There is another and much smaller group of patients in whom the tuberculous cavity remained limited to one or both upper lobes. These patients lived for many years with open cavities from whose sputum tubercle bacilli were always recovered. Yet, in spite of this, there was no spread of the disease to other parts of the lungs. These patients generally died of some disease other than tuberculosis and rarely showed evidence of intestinal or laryngeal tuberculsosis.

A comparative study of pulmonary tuberculosis before and after the advent of chemotherapy is beset by several difficulties. Chemotherapy and pulmonary tuberculosis are synonymous today, so that simultaneous comparative studies with untreated patients is not possible. The material presently at hand is that which is removed by resectional surgery which is becoming available in increasing amounts due to two factors: (1) As a result of prolonged chemotherapy in cases of pulmonary tuberculosis soon after its origin, the disease undergoes extensive resolution and the process is limited to a portion of a lobe or lung. (2) As a result of technical advances in thoracic surgery, portions of the lung can be removed with much greater facility. Thus the only comparative material is that which is available before the extensive use of chemotherapy. Much of this material is from autopsies although many surgical specimens are also available.

It is our opinion that when lung specimens of chronic pulmonary tuberculosis after antibiotic therapy are compared with those in which no such therapy was used striking differences are observed. In making this study we believe that it is important to compare cases of similar duration. A comparative study should answer the question as to whether the end results of healing are the same whether antibiotics are used or not.

The comparison between both groups is made

chiefly on surgically resected lesions. In some instances, however, autopsy material is utilized. Comparisons will be made of the cavity, encapsulated necrotic foci and the surrounding lung tissue.

TUBERCULOUS CAVITY (BEFORE CHEMOTHERAPY)

The development of the cavity occurs from a tuberculous pneumonia which has first undergone necrosis and then liquefaction. After the evacuation of the necrotic contents the cavity has a characteristic gross and microscopic appearance. The cavity which generally lies a few millimeters beneath the pleura has a thin wall in which three layers may be distinguished. The inner yellow layer is composed of nonliquefied necrotic fragments. The middle red zone is made up of tuberculous vascular granulation tissue. The outer grey layer, which represents the organized perifocal reaction, is surrounded by firm lung tissue, which represents perifocal reaction lying in the alveolar spaces. Characteristic of all tuberculous cavities is the fact that the inner necrotic lining of the cavity wall is continuous with the ulcer of the draining bronchus. The necrotic lining of the bronchial ulcer is also surrounded by a layer of granulation tissue. The partial destruction of the bronchus with narrowing of the lumen causes a check-valve mechanism at this site. This results in the mechanical enlargement of the cavity since more air enters the cavity than can escape.

Cavity Progression. In untreated cases as the disease advances there is concomitant healing. Progression of the disease may occur either from within the cavity or extension from without. The process from within is that the tubercle bacilli within the lumen bathe the cavity wall and a progressive necrosis results. When this occurs, the zone of granulation tissue and part of the outer wall of fibrosis become incorporated within the necrotic zone. Although the nuclei in these layers have become disintegrated, the former structure of these zones is still discernible. Concomitant with the progressive necrosis a new layer of vascular granulation tissue forms around it and beyond this a new area of perifocal reaction develops.

The process from without is that new areas of tuberculous pneumonia may develop in the immediate proximity of the cavity and extend to involve it in the necrotic process. It may liquefy and pour its contents into the lumen of the cavity.

Thus as a cavity grows older there is progression both from within and without. There is a concomitant repair of these areas of progression in the form of new granulation tissue and organization of the recently developed areas of perifocal reaction. The thickness of the cavity wall is dependent upon the extent of organized perifocal reaction which occurs over a period of time. The new areas of activity occur irregularly within the cavity wall. As a result of this the thickness of older cavities is irregular.

Cavity Healing. Spontaneous healing of tuberculous cavities may occur without the aid of collapse therapy although it is extremely difficult to obtain a true incidence of this occurrence. The closure and healing of tuberculous cavities has occurred with much greater frequency as a result of the various forms of collapse therapy. Healing with obliteration of the cavity lumen is well documented in the literature.[1–26] In the days prior to chemotherapy the pathologist's experience with these lesions was obtained chiefly from autopsy material since resectional surgery for tuberculosis preceded the use of antibiotics by a short period. Death in these cases was often due to a cause other than tuberculosis.

Healing of a tuberculous cavity may occur in one of two ways: (1) With obliteration of the lumen and (2) with the lumen of the cavity remaining open.

1. *Healing with obliteration of the lumen:* We have previously pointed out that this is by far the more frequent form of cavity healing.[19] The end result of this type is either an inspissated (filled-in) cavity or a radial scar. Healing of this form occurs by the approximation of the ulcerated bronchial surfaces at the bronchocavitary junction. Collapse therapy does much in these cases to bring this about. Following the approximation of the bronchial surface, proliferation of granulation tissue in this region continues until the apposing surfaces join and the lumen is obliterated. If the granulating surfaces unite firmly, the occlusion will be lasting and the cavity permanently closed. In all instances in which an inspissated cavity or a radial scar exists, the draining bronchus ends blindly either in the wall of the cavity or in an area of fibrosis connecting with the wall of the inspissated cavity.

After closure of the bronchus the cavity wall contracts quite rapidly. Since most cavities contain large necrotic masses within the lumen and along the inner wall, these become inspissated and form the core of the obliterated cavity. Simultaneously, the wall of the cavity through an increase of collagen fibrils, is converted into a zone of hyalinized connective tissue. This in turn is surrounded by a wider area of loose connective tissue which represents the organized perifocal reaction. This zone is generally wide because in most instances the cavity closed after the tuberculous process had been present for some time. As we have already stated, the width of the cavity wall is dependent upon the extent of the organization of perifocal reaction and that this increases with the age of process. Collapse therapy aids in the thickness of the cavity wall by entrapping the perifocal reaction within the alveoli.

Radial scars generally result when at the time of the closure of the cavity there are only a few necrotic fragments within the cavity lumen. After the space is obliterated the granulation tissue invades and replaces the necrotic material. Subsequently, the granulation tissue is converted into connective tissue. As this occurs there is a contraction of the tissues forming the cavity which results in a radial scar. The peripheral portions of the scar taper off among the surrounding alveolar septa, which they thicken. The contraction also results in a stretching and tearing of the surrounding alveolar septa leaving dilated air sacs, often with bleb formation.

2. *Healing with an open cavity—open-healing:* The healing of such cavities may occur in the presence of draining bronchi which open widely into the cavity lumen. Although there are isolated reports in the literature,[4,19,20,27–30] these cases are rare indeed. There are two components to this form of cavity healing: (1) the complete shedding of the inner necrotic zone manifested clinically by the disappearance and persistent absence of tubercle bacilli from the sputum; (2) the transformation of the tuberculous granulation tissue of the cavity wall into a non-specific fibrous tissue.

In the days prior to chemotherapy we observed only two cases of open healing in over 2,000 autopsies on individuals with chronic pulmonary tuberculosis. The inner surface of these cavities is lined by a smooth, grey or red surface and their walls are thick. The bronchi opening into these cavities are widely patent and their lining membrane is smooth and grey.

Microscopically, the development of healing changes in the walls of cavities is the same in "open" as in "closed" healing types. There is a gradual transformation of the wall into fibrous tissue at the expense of the specific tuberculous elements.

One of the two cases showed an epithelialized surface while the other wall was composed only of connective tissue. The cavity walls in both instances were thick.

TUBERCULOUS CAVITY (AFTER CHEMOTHERAPY)

The administration of drugs is generally begun after the tuberculous cavity has been present for some time. It is our opinion that there are striking changes brought about by the use of antibiotics and are as follows: (1) clearing of the perifocal reaction; (2) effect on the progression of the cavity; (3) more rapid healing of the cavity wall; (4) re-epithelialization of the bronchus at the bronchocavitary junction with extension into the inner wall of the cavity; (5) more frequent inspissation of cavity contents and (6) more frequent "open" healing.

Clearing of the Perifocal Reactions. We have previously shown that one of the most readily observed changes following chemotherapy is to reduce perifocal reaction to a minimum.[31] This observation has been confirmed by others.[32,33] Most of the clearing of the shadows observed in serial roentgenograms following the institution of therapy is the result of the dissolution of the perifocal reaction.

It is obvious that the best effect can be obtained when the drugs are administered before the extensive organization of the perifocal reaction has taken place. Thus the third or outer layer of the cavity wall is either extremely thin or, in some instances, absent. (Fig. 1*a*.) The thinness of this layer depends upon the nearness which the drugs were first given after the formation of the cavity. Similar untreated cases will show a variably wide alveolar filling process, cellular in its inner aspect and serous in the peripheral parts. (Fig. 1*b*.)

Comparing treated and untreated cavities of similar anatomic age, the chemotherapeutically treated cavity is much thinner with an area of resilient lung tissue lying between it and the

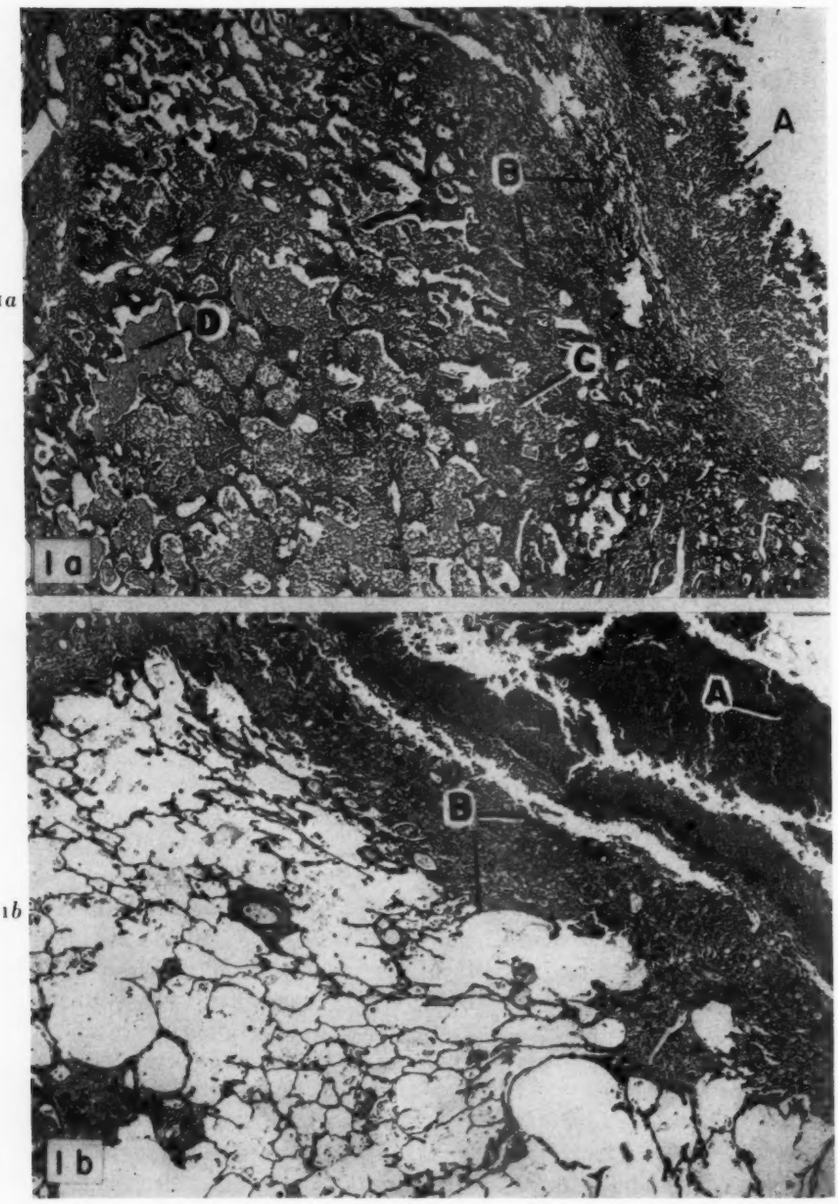


FIG. 1. (*a*) The patient was a fifteen year old Negro girl who died several months after the onset of pulmonary tuberculosis. She had had no chemotherapy during her illness. At autopsy her lungs in addition to multiple cavities showed large areas of tuberculous pneumonia undergoing necrosis. The intestinal tract was the seat of deep tuberculous ulcers from the ileum to the rectum. Photomicrograph of a cavity wall and surrounding zone shows a wide perifocal reaction. The inner necrotic zone (A) is surrounded by a narrow layer of tuberculous granulation tissue (B). The inner part of the perifocal reaction is cellular (C), while the outer and wider portion is serous (D). (*b*) A twenty-four year old white man was admitted to the hospital seven months prior to his death in a semi-comatose state. A diagnosis of tuberculous meningitis was established. Roentgenograms showed a large cavity in the upper lobe of the right lung. He was immediately put on streptomycin, 1 gm. daily, and intrathecal streptomycin, 50 mg. every other day. He received a total of 296 gm. of streptomycin up to the day of his death. He died of sequelae of healing tuberculous meningitis. Photomicrograph of the cavity wall shows an inner zone of necrotic material (A). The layer of vascular granulation tissue beyond it (B) is of variable width. The empty alveolar spaces bordering the cavity, from which the perifocal reaction has been cleared as a result of the antibiotics, accounts for the thinness of the cavity wall.

overlying pleura. The cavity wall in the untreated cases is much thicker and often blends with a thickened, overlying pleura. (Fig. 2.)

Effect on the Progression of the Cavity. The administration of the drugs very soon alters the course of the tuberculous cavity. In untreated cases healing changes keep pace with progression. Progression, as we have already stated, occurs from within or without the cavity. There is both macroscopic and microscopic evidence that progression is halted. This is seen in absence of signs of progression from within and also the absence of new tuberculous foci rupturing into the lumen of the cavity. Further evidence is seen in the lack of formation of new perifocal reaction around the cavity wall, new perifocal reaction indicating new activity in the tuberculous cavity.

More Rapid Healing of the Cavity Wall. We believe that this is difficult to assess. The evaluation can be made only by knowing the approximate age of the cavity (from clinical studies) and by determining whether the healing changes are greater than those of similar age in untreated cases. These changes must be striking and out of proportion to the age of the cavity, because healing changes occur in the natural course of the disease. Thus the healing changes in the cavity wall, as evidenced by collagen connective tissue, are far out of proportion to what would be expected in cases such as those which had not had the benefit of chemotherapy.

Re-epithelialization of the Bronchus at the Bronchocavitary Junction. The outstanding feature of drug therapy in tuberculosis is the healing of tuberculous ulcers with re-epithelialization. The drugs thus appear to exert their greatest effect of superficial surfaces. The necrotic lining of the bronchus at this site is replaced by the granulation tissue. The epithelial regeneration occurs from the intact epithelium just proximal to the ulcer. The regenerated epithelium is generally flattened or squamous in character and extends onto the inner wall of the cavity for variable distances. (Fig. 3*b*.) It generally stops where the cavity wall is lined by a pyogenic or a necrotic surface. We have never seen regeneration occur over a necrotic surface.

More Frequent Inspissation of Cavity Contents. It is our opinion that the re-epithelialization disrupts the check-valve mechanism which existed at the entrance of the ulcerated bronchus into the cavity and which allowed more air to enter than to leave the cavity. As a result of this, distention of the cavity no longer occurs, and contraction of granulation tissue in its wall results in decreased size of the cavity. As the granulation contracts, the caseous contents within the cavity lumen become inspissated. The fluid within the necrotic débris is absorbed. As the process of healing continues, calcium salts are deposited in the necrotic zone and the zone of granulation tissue is gradually converted into hyaline connective tissue.

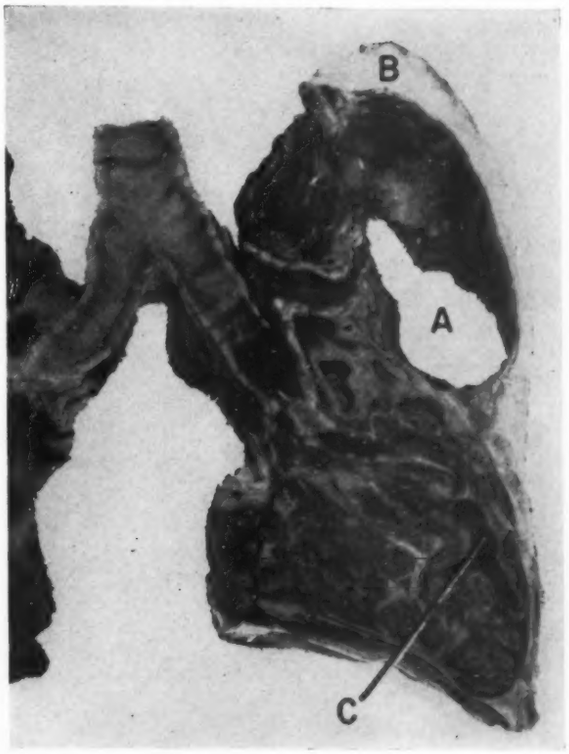
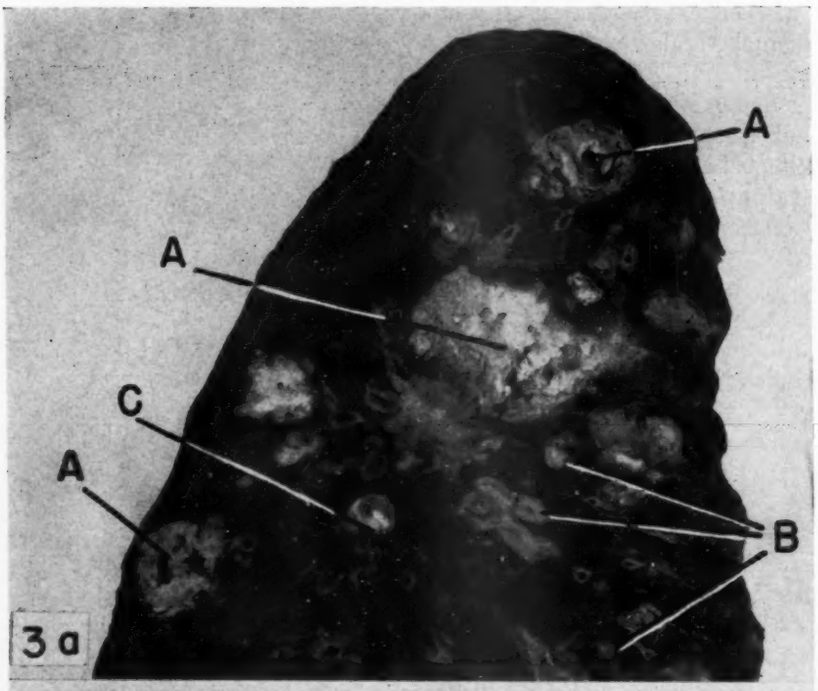


FIG. 2. The patient was a twenty-seven year old white man whose onset of pulmonary tuberculosis began several years prior to his death. He received no chemotherapy. Coronal section of the lung shows a thick-walled cavity occupying almost all of the right upper lobe (A). The greatly thickened pleura (B) fuses with the cavity wall. The right lower lobe, which shows large areas of fibrosis, is the seat of bronchiectasis (C).

The end result in these cases is an inspissated cavity with a communicating bronchus. (Fig. 3*a* and *b*.) Comparing the healed cavity after chemotherapy with that healed without the use of drugs, it is found that in treated cases the bronchus is patent, while in those untreated no bronchial communication can be demonstrated.[34]

It is not an unusual experience to find that a

3a



3b

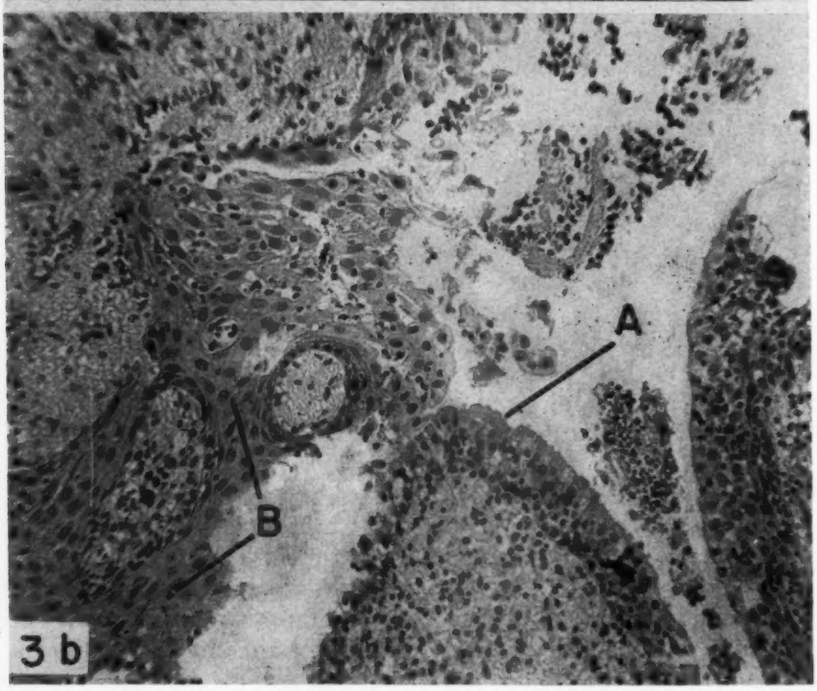


FIG. 3. (*a*) The patient was a twenty-four year old white man whose onset of pulmonary tuberculosis was two and a half years before his right pneumonectomy. Chemotherapy was begun within the same month as the onset of his illness and continued up to the day of his operation. The course and regimen of the drugs varied during this period. The drugs utilized were streptomycin, PAS, INH and viomycin. A coronal section of the right lung shows the lung occupied by numerous individual necrotic foci. Some of these represent inspissated (filled-in) cavities (A). Others are encapsulated, caseous foci which had never liquefied (B); some of these contain calcium salts (C). The capsules around all the necrotic foci are thin. There is an absence of pulmonary fibrosis and emphysema. In spite of extensive disease, the lung is not greatly reduced in size. (*b*) Photomicrograph of the bronchocavitary junction of one of the inspissated cavities in Figure 3(*a*) shows the columnar epithelium of the intact bronchus (A). That which lines the adjoining cavity is thick squamous in character (B). The epithelium of the cavity lies on granulation tissue.

cavity, which by roentgenographic studies had been observed to close, will subsequently show an annular shadow at the same site. We have observed secondary liquefaction of the inspissated, necrotic contents within the lumen of the cavity. It is our impression that neutrophils are secreted into the bronchial lumen and extend into the inspissated cavity among the calcified necrotic fragments. This results in a sequestration, liquefaction and evacuation of the cavity contents.

In the light of the above observations, the important question arises as to whether the inspissated cavity with a patent bronchus is a potential source of danger. Extensive microbiologic studies have been and are being carried out to answer this question.[35–45]

More Frequent "Open" Healing. Open healing is observed with increasing frequency after long-term chemotherapy. We believe that this form of healing may occur after evacuation of an inspissated cavity or there may be open healing from the onset, the latter being the more frequent mode of healing. The end result is the same in either form.

Re-epithelialization of the bronchus is undoubtedly an important factor in the increased incidence of this form of healing. In untreated cases the check-valve mechanism results in a retention of the necrotic contents within the cavity. As a result of the healing of the ulcerated bronchial surface and re-epithelialization wider drainage is now possible.

Healing of these cavities occurs through the invasion of the necrotic lining by the surrounding vascular granulation tissue. In occasional instances the epithelium may extend from the bronchus along the inner wall of the cavity on the granulation tissue. Subsequently, with the increase of collagen, the granulation tissue is converted into hyaline connective tissue. These cavities communicate with bronchi.

ENCAPSULATED NECROTIC FOCI

These represent areas of tuberculous pneumonia which have undergone necrosis but have not become liquefied. One of the factors which determines the development of liquefaction and cavity formation is the size of the focus although this does not appear to be the only factor. Generally, the smaller the size of the original area of tuberculous pneumonia, the greater is the chance for encapsulation.

As the area of tuberculous pneumonia undergoes necrosis there is a concomitant development of tuberculous granulation tissue at its periphery. The granulation tissue encloses the necrotic zone completely and in our experience no bronchi communicate with it. If bronchi were to communicate with these, there would always be the possibility that they are a possible source of danger. It has been our experience that the entrance of neutrophils, which liberate the proteolytic enzymes necessary to liquefy necrotic foci, may come through the lumen of the bronchus.

The zone of granulation tissue and perifocal reaction around the necrotic center are similar to that present in the cavity wall. As the process of healing continues, the granulation tissue is converted into hyalinized, connective tissue forming the inner part of the capsule, while that portion of the perifocal reaction which is not eliminated becomes organized into an outer and wider zone of loose connective tissue. The ultimate fate of the perifocal reaction depends upon the patency of the draining bronchi and lymphatic channels proximal to these involved areas. If the bronchi and lymphatic vessels are clear, the peripheral portion is either expectorated or absorbed by the lymphatic channels. Collapse therapy, by its compression of the bronchi and lymphatic channels, prevents the elimination of the perifocal reaction and thus results in more extensive organization of the perifocal reaction.

Contraction of the necrotic foci results in a stretching and tearing of the surrounding alveolar septa with the formation of emphysematous areas in these regions. Bleb formation generally occurs around the larger foci.

Encapsulated Necrotic Foci after Chemotherapy. The essential change brought about by antibiotics is in the thickness of the capsule. As a result of the clearing of the perifocal reaction, there is either only a very narrow or no loose connective tissue zone around the inner hyalinized connective tissue capsule. The inner hyalinized zone is of a width similar to that in cases in which no antibiotics were employed and represents the end-stage of the tuberculous process. Thus healed encapsulated, caseous foci showing the favorable effect of chemotherapy are different from similar healed necrotic areas without drugs in that the outer loose connective tissue capsule of the latter is thicker. (Fig. 3*a*.)

Pulmonary Fibrosis and Emphysema Resulting from Tuberculous Foci. The basic tuberculous process in the lung takes place in the alveolar spaces and results in a tuberculous pneumonia. Generally, the smaller the size of these foci, the greater will be the opportunity for organization of the pneumonia. This is best seen in the acinous nodose foci where the process develops in the lung tissue beyond the terminal bronchiole. It also occurs in areas where the tuberculous pneumonia occupies only a small part of a lobule. Organization of the tuberculous pneumonia occurs before the development of necrosis. The fibrinocellular exudate within the alveoli is invaded by fibroblasts, epithelioid cells, Langhans' giant cells and collagen fibers. These elements replace the exudate and are attached to the surrounding alveolar septa which are thickened by similar cells. As the collagen fibers increase at the expense of the cellular elements, an irregular area of fibrosis remains which is surrounded by stretched and torn alveolar septa.

Pulmonary fibrosis may also replace smaller necrotic foci. The zones of granulation tissue around the necrotic foci gradually invade and replace the caseous centers. As the collagen fibers increase in number, they compress and replace the surrounding cells and capillaries of the granulation tissue. As the granulation tissue is transformed into connective tissue, there is a gradual contraction of the focus. Thus the end-result is an irregular scar smaller than the necrotic focus which it replaces. As the focus contracts it stretches the surrounding alveolar septa to which it is attached, resulting in a perifocal emphysema.

Emphysema in pulmonary tuberculosis is a concomitant part of the destruction and resultant contraction of the lung parenchyma. Thus as the tuberculous process progresses with necrosis and surrounding fibrosis a compensatory dilatation of the surrounding air sacs develops. Since the lung parenchyma is a contiguous elastic structure, any replacement of it must be compensated by the surrounding intact portion. This is done by a stretching of the surrounding elastic fibers. When the thinned fiber cannot stretch far enough, it ruptures.

Pulmonary Fibrosis and Emphysema after Chemotherapy. There is an over-all decrease in the amount of fibrosis and emphysema in patients who have received chemotherapy over a long period of time when compared with cases of similar duration in which the patients received no drug chemotherapy. This is true particularly when the drugs have been given soon after the onset of the illness. This decrease is due both to the elimination of the perifocal reaction resulting in decreased fibrosis and to the fact that in prolonged chemotherapy dissemination is minimal or absent. We have been impressed with the fact that there are many less non-necrotic tuberculous foci after chemotherapy than in non-treated patients. Acinous nodose foci, a common tuberculous lesion before chemotherapy, are an extremely infrequent finding. Thus there are two important ways in which the development of pulmonary fibrosis in pulmonary tuberculosis is greatly reduced by the use of antibiotics.

Emphysema, which results from the contraction resulting in the formation of fibrosis, is also diminished as a result of the prolonged use of antibiotics. The extent of the emphysematous areas around necrotic foci and in subpleural regions is far less than in comparable cases which have not had the benefit of chemotherapy.

As a result of the greatly lessened pulmonary fibrosis and emphysema in patients receiving prolonged chemotherapy there is a greater lung volume than in similar untreated patients. Intact lung parenchyma which rarely contains scars widely separates the necrotic foci. (Fig. 3*a*.)

CONCLUSIONS

Pulmonary tuberculosis is greatly altered by the prolonged use of antibiotics. Inspissated cavities are observed with much greater frequency than in the prechemotherapy era. Re-epithelialized bronchi communicate with these cavities. The walls of the cavities are thinner than those of similar ages which have received no antibiotics. Necrotic foci are also surrounded by thinner capsules than foci of similar ages not having the benefit of chemotherapy. The decreased thickness of the areas of fibrosis around the cavities and necrotic foci is the result of the elimination of the perifocal reaction. Open healing of tuberculous cavities occurs more frequently under the influence of prolonged chemotherapy. The end-result in such cases is a relatively thin cavity wall composed of hyalinized connective tissue with a complete loss of specific tuberculous elements

Much less frequently is there epithelialization of such cavity walls.

Pulmonary fibrosis and emphysema are greatly lessened as a result of the prolonged use of antibiotics, thus a lessened decrease in the lung volume.

Acknowledgment: The author gratefully acknowledges the cooperation of the Medical Illustration Departments of the Veterans Administration Hospital, East Orange, N. J., the Veterans Administration Hospital, Brooklyn, N. Y. and Sea View Hospital, Staten Island, N. Y.

REFERENCES

1. Hansemann, D. Über Heilung und Heilbarkeit der Lungenphthise. *Klin. Wchnschr.*, 39: 745, 1902.
2. Hart, C. Über die Heilbarkeit und Heilung tuberkulöser Lungenkavernen. *Ztschr. f. Tuberk.*, 35: 253, 1922.
3. Bacmeister, A. Das Kavernenproblem in seiner klinischen Bedeutung, *Beitr. z. Klin. d. Tuberk.*, 67: 157, 1927.
4. Huebschmann, P. Pathologische Anatomie der Tuberkulose. Berlin, 1928. Julius Springer.
5. Gilbert, M. Deux observations anatomo-cliniques concermant la guerison de cavernes tuberculeuses du poumon. *Rev. de la tuberc.*, 12: 979, 1931.
6. Coryllos, P. N. How do rest and collapse treatment cure pulmonary tuberculosis? *J. A. M. A.*, 100: 480, 1933.
7. Sweany, H. C. The changes of pulmonary tuberculosis as a result of treatment. *Am. Rev. Tuberc.*, 32: 544, 1935.
8. McPhedran, R. M. and Long, E. R. Clinical and pathologic notes on a case of healed pulmonary tuberculosis. *Arch. Path.*, 20: 168, 1935.
9. Graeff, S. Die Kaverne der Lungentuberkulose vom pathologisch-anatomischen Standpunkt aus. *Ergebn. d. ges. Tuberk-Forsch.*, 7: 257, 1935.
10. Amberson, J. B. The process of resolution in pulmonary tuberculosis. *Am. Rev. Tuberc.*, 33: 269, 1936.
11. Jacquerod, M. The Natural Processes of Healing in Pulmonary Tuberculosis. Translated by J. D. Sinclair. New York, 1926. William Wood and Co.
12. Tchertkoff, I. G. and Bobrowitz, I. D. Spontaneous closure of tuberculous pulmonary cavities. *Quart. Bull. Sea View Hosp.*, 1: 173, 1936.
13. von Karwowski, J. Pathologisch-anatomische Beiträge zur Frage der aktiven Behandlungsmethode der grossen und pleuranahen tuberkulösen Kaverne. *Beitr. z. Klin. d. Tuberk.*, 89: 59, 1937.
14. Derscheid, G. and Toussaint, P. Necroses tuberculeuses et cavernes pulmonaires, processes de guérison. *Presse méd.*, 45: 1739, 1937.
15. Pinner, M. Pathology of Pulmonary Collapse. In Alexander's The Collapse Therapy of Pulmonary Tuberculosis. Springfield, Ill., 1937. Charles C Thomas.
16. Roberts, L. and Pagel, W. Behaviour of tuberculous cavities in the lung under artificial pneumothorax treatment. *Brit. M. J.*, 2: 1258, 1938.
17. Wurm, H. Pathologische Anatomie d. Heilungsvorgaenge b. d. Tuberkul. Lungenkaverne. In Hein-Kremer-Schmidt, Kollapstherapie der Lungentuberkulose, p. 33, Leipzig, 1938. Thieme.
18. Pagel, W. and Simmonds, F. A. H. The healing of cavities. *Am. J. M. Sc.*, 197: 281, 1939.
19. Auerbach, O. and Green, H. The pathology of clinically healed tuberculous cavities. *Am. Rev. Tuberc.*, 52: 707, 1949.
20. Pinner, M. Healing of tuberculous cavities. *Am. Rev. Tuberc.*, 42: 731, 1940.
21. Shamaskin, A. Inspissated cavity. *Am. Rev. Tuberc.*, 44: 310, 1941.
22. Pagel, W. and Simmonds, F. A. H. Cavity healing and bronchial occlusion. *Am. J. M. Sc.*, 203: 177, 1942.
23. Bobrowitz, I. D. The round pulmonary tuberculous focus. *Am. Rev. Tuberc.*, 47: 472, 1943.
24. Loesch, J. Closure of tuberculous cavities. *Am. Rev. Tuberc.*, 50: 500, 1944.
25. Loesch, J. Closure and healing of tuberculous cavities. *Am. Rev. Tuberc.*, 58: 322, 1948.
26. Study, R. S. and Morgenstern, P. Prognosis of inspissated cavities. *Am. Rev. Tuberc.*, 59: 53, 1949.
27. Saugman, C. Dauerfolge der Pneumothoraxbehandlung bei Lungentuberkulose. *Ztschr. f. Tuberk.*, 34: 425, 1931.
28. Pagel, W. Zur Enstehungsgeschichte und Kausistik der Lungentuberkulose. *Beitr. z. Klin. d. Tuberk.*, 79: 383, 1931–32.
29. Alexander, H. Zum Problem der Tuberkulosen Kaverne. *Beitr. z. Klin. d. Tuberk.*, 86: 424, 1935.
30. Pagel, W. and Robinson, H. J. Spontaneous cavity healing. *Papworth Res. Bull.*, 1: 37, 1936.
31. Auerbach, O. and Stemmermann, G. N. Anatomic changes in tuberculosis following streptomycin therapy. *Am. Rev. Tuberc.*, 58: 449, 1948.
32. Mahon, H. Pathology of pulmonary tuberculosis: as modified by streptomycin therapy. *Am. Rev. Tuberc.*, 61: 543, 1950.
33. Silverthorne, M. D. and Silverman, G. The effect of streptomycin on the morphology of the tuberculous lesion. *Am. Rev. Tuberc.*, 61: 525, 1950.
34. Auerbach, O., Katz, H. L. and Small, M. J. The effect of streptomycin therapy on the bronchocavitary junction and its relation to cavity healing. *Am. Rev. Tuberc.*, 67: 173, 1953.
35. O'Brien, E. J., Miller, A. C., Chapman, P. T., Koster, K. and O'Rourke, P. V. The present chaos regarding resection of residual caseous lesions in pulmonary tuberculosis. *J. Thoracic Surg.*, 26: 441, 1953.
36. D'Esopo, N. D., Ryan, B. J. and Medlar, E. M. Prolonged therapy with streptomycin—PAS. A clinical-pathological correlation, p. 78. Tr. of 10th Conference on Chemotherapy of Tuberculosis, held under the Auspices of the U. S. Veterans Administration, Army and Navy, Jan. 25–28, 1951.
37. Ryan, B. J., Medlar, E. M. and Welles, E. S. Simple excision in the treatment of pulmonary tuberculosis. *J. Thoracic Surg.*, 23: 327, 1952.

38. D'Esopo, N. D., Bernstein, S. and Decker, A. M., Raleigh, J. W. and Steenken, W., Jr. Bacteriology of lesions resected during chemotherapy, p. 228. Tr. of 12th Conference of Chemotherapy of Tuberculosis, held under the auspices of the U. S. Veterans Administration, Army and Navy, Feb. 9–12, 1953.

39. Medlar, E. M., Bernstein, S. and Steward, D. M. A bacteriologic study of resected tuberculous lesions. *Am. Rev. Tuberc.*, 66: 36, 1952.

40. Steenken, W., Jr. and Wolinsky, E. Methods of determining the viability of tubercle bacilli, a critique, p. 269. Tr. of 12th Conference on Chemotherapy of Tuberculosis, held under the auspices of the U. S. Veterans Administration, Army and Navy, Feb. 9–12, 1953.

41. Steele, J. D., Narodick, B. G. and Cadden, A. V. The influence of long-term chemotherapy on the surgery of pulmonary tuberculosis. *J. Thoracic Surg.*, 26: 459, 1953.

42. Granville, G. E., Jenkins, D. E., Cooley, D. A., De Bakey, M. E., Whitcomb, F. C. and Halpert, B. Cultural properties of M. tuberculosis in resected pulmonary lesions of patients treated with streptomycin and para-aminosalicylic acid. *Am. Rev. Tuberc.*, 68: 727, 1953.

43. Falk, A., Kaufman, J. E. and Tucker, W. B. Resectional surgery in pulmonary tuberculosis, with a bacteriologic study of the resected tissue, p. 216. Tr. of 12th Conference on Chemotherapy of Tuberculosis, held under the auspices of the U. S. Veterans Administration, Army and Navy, Feb. 9–12, 1953.

44. Dubos, R. J. and Hirsch, J. G. The antimycobacterial activity of a peptide preparation derived from calf thymus. *J. Exper. Med.*, 99: 55, 1954.

45. Hobby, G. H., Auerbach, O., Lenert, T. F., Small, M. J. and Comer, J. V. The viability of tubercle bacilli in tuberculous lesions following chemotherapy. *Am. Rev. Tuberc.*, 70: 191, 1954.

Mechanisms of Fatal Pulmonary Hemorrhage in Tuberculosis

J. Robert Thompson, M.D., *Chicago, Illinois*

Fatal hemorrhage is not an uncommon cause of death in patients afflicted with pulmonary tuberculosis. Perhaps the most disturbing feature is that many of the individuals who are stricken have passed the acute phase of their illness and apparently are on the road to recovery.

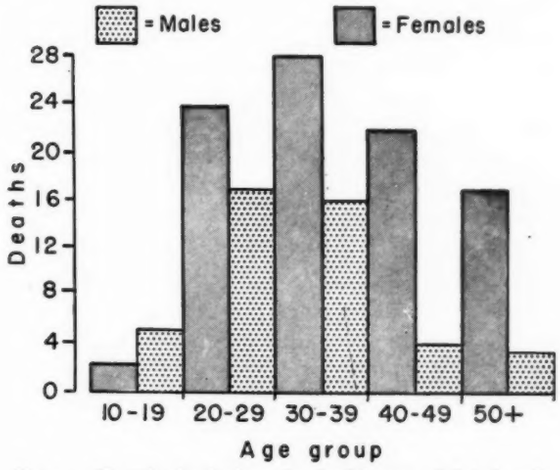


Fig. 1. Graph depicting the incidence of fatal pulmonary hemorrhage according to age and sex.

The incidence of fatal hemorrhage has been estimated by different authors to be from 1 to 5 per cent.[1] A survey of 2,830 autopsies at the Municipal Tuberculosis Sanitarium revealed that 138 cases (4.87 per cent) died in this manner. Of this total, ninety-three were men and forty-five were women, and the greatest incidence was in the age group thirty to thirty-nine years. (Fig. 1.) The youngest and oldest individuals to suffer fatal hemorrhage were eleven and sixty-five years of age, respectively. Of the 138 only 57 gave a history of having had any previous bleeding or hemorrhage. The chronicity of the disease was certainly a factor, the interval of time varying from one month to twenty-one years, and thirty-three patients gave a history of having had the disease for a period of four years or over. Twenty-eight had pneumothorax for varying lengths of time, the maximum being four years; however, their disease was of such a nature that in only a few instances was any beneficial effect noted clinically and no relationship to hemorrhage could be shown. The most common complication was amyloidosis; thirty-one cases (22 per cent) showed gross

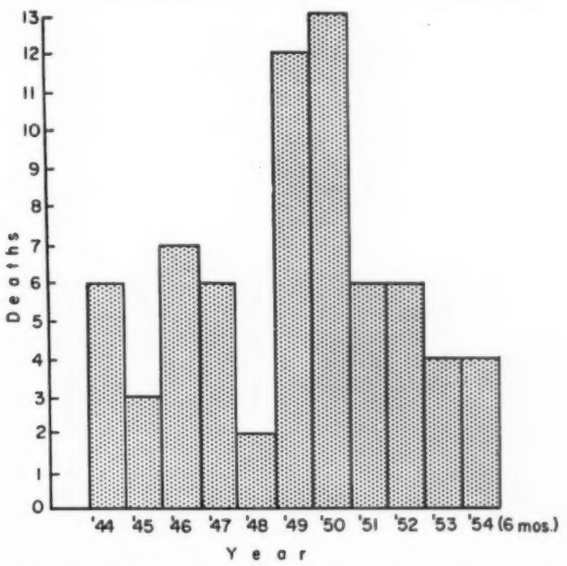


Fig. 2. Graphic comparison of the number of deaths from fatal pulmonary hemorrhages during the last ten years.

and/or microscopic evidence of amyloid degeneration (this is about the same percentage as is seen routinely in our autopsy work). There was one case each of hypertensive heart disease, chronic glomerulonephritis, syphilis, silicosis, nutritional cirrhosis and cor pulmonale with failure.

There is no chronologic pattern as to the occurrences of these fatal hemorrhages. For example, in the years 1933, 1934 and 1935 several were recorded, and the next comparable number was in the middle 1940's; however, the highest total for any single year occurred in 1950. (Fig. 2.) In spite of the chemotherapeutic and surgical measures employed in the

past few years the incidence of fatal hemorrhage has remained about the same. Since chronicity is a factor it stands to reason that procedures which prolong the course of the disease also increase the likelihood of sudden fatal hemorrhage. This is especially true in cases which are far advanced at the time of admission to the sanitarium. One cannot discount the observations of Petersen[7] in which he correlated hemorrhagic episodes in the tuberculous patient with conditional changes in the meteorologic environment. These episodes he associated with blood pressure increases attributable to pressor changes.

One usually associates fatal pulmonary hemorrhage with the rupture of an artery adjacent to or a part of a parenchymal cavity wall following an aneurysmal dilatation. These dilatations have been termed Rasmussen's aneurysms as Dr. Vald Rasmussen was the first to describe them in 1868.[9] The number of these lesions identified varies greatly in different institutions and perhaps to some extent in proportion to the time spent dissecting the specimens. Proliferative and reparative processes usually prevent aneurysmal formation within tuberculous cavities by occluding the blood vessels before their walls are destroyed. Because of the magnitude of the hemorrhage and the destructive and/or reparative processes going on in the lung, it is almost impossible to demonstrate the site of bleeding. This is especially true in those cases in which the bleeding apparently results from the rupture of an aneurysm; whereas bronchial lesions which perforate or erode the adjoining vessel can be demonstrated with relative ease. Rasmussen pointed out in his article that many men before him had attempted to explain the causes and mechanisms of fatal pulmonary hemorrhage but had been rather unsuccessful in their attempts. Laennec supported the idea that frequently pulmonary hemorrhage came about by a diapedesis of blood through the bronchial mucus membranes. A factor favoring this theory was that vessels in the vicinity of the cavity, especially in the fibrous wall, were usually obliterated. This was true also for vessels which traversed the cavity; however, we know now that many of these vessels remain open. Andral was of the opinion that there were three possible sources of pulmonary hemorrhage; first, that seen in conjunction with a tuberculous endobronchitis; however, he was not in a position to demonstrate the actual bleeding point; second, bleeding in cases of pulmonary apoplexy (it is assumed that by this he meant vascular disturbances such as hemorrhagic infarctions) and third, hemorrhage from a cavity. In this instance Andral was able to demonstrate a bleeding vessel in only one case—a vessel that was enclosed in a trabeculum crossing the cavity.

Rokitansky was about the only writer who had described cases such as simulated those of Rasmussen. According to Rokitansky the copious hemorrhages seen in tuberculosis arose from branches of the pulmonary arteries situated in the condensed walls of cavities, especially bronchiectatic cavities. He was of the opinion that the vessel walls became macerated, jelly-like and soft due to exposure to the contents of the cavity and necrotic processes in the wall of the cavity so that finally they would burst and a massive hemorrhage would take place. The lesion he described as either a split-like fissure in the vessel or the separation of a portion of the vascular wall gave rise to a punched-out defect. Very frequently this punched-out defect was seen in an aneurysmal dilatation of the vessel toward the cavity.

Rasmussen's observations were based on the examination of eleven patients who died during a violent hemoptysis. Eight of these were patients in whom there was a rupture of a vessel running in the wall of the cavity and the other three were instances of rupture of an aneurysm of the aorta into the bronchus or into the pulmonary tissue itself. Of the eight cases in which hemorrhage was due to a rupture of a vessel adjacent to a cavity, four demonstrated rupture of a small sac-like aneurysm which had developed on a branch of a pulmonary artery running in the wall of the cavity, and four showed dilatation or ectasia of a branch of the pulmonary artery with operculated rupture. These aneurysms varied in size from that of a pea to a walnut. The wall varied in thickness and in those which had not ruptured the wall was seen to be two or three times thicker than the rest of the vessel. The lesions were sometimes multiple and the vessels on which the aneurysms were located averaged from 1 to 3 mm. in diameter.

Plessinger and Jolly[8] studied a series of 667 cases from the years 1938 to 1947 and of these forty-nine died of massive pulmonary hemorrhage. In twenty-nine of these cases

they were able to demonstrate an aneurysmal dilatation of a vessel. On the basis of their histologic studies, they describe the incriminative vessel as usually running tangential to the wall of the cavity. As the vessel broached the wall of the cavity it passed through its own diseased pulmonary tissue and started to dilate slightly. Concomitantly a variable degree of endothelial thickening usually occurred so that the lumen of the vessel was slightly constricted. Similar obliterative endothelial changes were observed in the other large vessels in the vicinity of the cavity wall. Serial sections revealed that the vessel wall proper dilated eccentrically; the dilatation taking place only on the side toward the lumen of the cavity. Finally a point of rupture of the media was encountered. A great deal of emphasis is placed on the presence of a fibrin clot in every unruptured aneurysm and in some of the ruptured aneurysms. They are in agreement with Rasmussen's theory that this clot may occasionally plug the rent in the aneurysmal sac and thus prevent a fatal hemorrhage for some time.

O'Leary[6] reported a death occurring in a nine month old infant in which instance a recently ulcerated cavity eroded a large vessel. Certainly some of the cavities seen appear to be so rapidly excavating that proliferative changes in the neighboring blood vessels do not take place.

Codina Suque and Mansilla Delicado[1] believed that bleeding might be the result of a profuse diapedesis of blood into the alveolar spaces quite removed from an active tuberculous process, or at least from an ulcerating lesion. They were of the opinion that what was commonly considered to be posthemorrhagic "seeding" probably represented hemorrhagic areas complicating pre-existing tuberculous foci. The pre-existing tuberculous involvement we would assume to have been a recent bronchogenic or hematogenous dissemination from a "spilling" lesion elsewhere in the parenchyma or lymph nodes. These workers emphasize that it is not necessarily the amount of blood lost but the impingement on functional lung parenchyma which accounts for death.

Quiroga[4] points out that fatal hemorrhage may be the result of a rapidly ulcerating caseous pneumonia (necrotic pneumonia of Sabourin) or from a rupture of small vessels constituting the vascular make-up of cavity walls. However, we have not seen sufficient evidence of bleeding from granulation tissue such as lines most tuberculous cavities to account for a fatal hemorrhage in any of the cases studied. Klosk[3] reported a case of fatal hemorrhage due to rupture of a large branch of the pulmonary artery without aneurysmal formation—a circumstance he considered unique.

FIG. 3. Section through the lung showing Rasmussen's aneurysm in the medial portion of a cavity surrounded by dark red clotted blood. A small rent was found in the wall of the aneurysm which was responsible for the fatal hemorrhage.

The inconsistency of the mechanism of fatal hemorrhage can best be illustrated by the following case reports:

CASE REPORTS

CASE 1. E. S., a forty-three year old Negro man, was admitted to the sanitarium approximately one year after the onset of his illness. He had been "streaking" for three weeks prior to admission and on the second hospital day he suffered a severe hemorrhage and expired one hour later.

Pathologically, the lungs were emphysematous and on section multiple cavities were seen. There was a 3.5 cm. cavity in the upper portion of the right lung which had a heavy-walled aneurysm 1.5 cm. in diameter within it. (Fig. 3.) Careful dissection revealed a rupture

FIG. 4. A section through the left lung showing a large cavity in the apex filled with clotted blood and a small cavity in the mid-portion with a probe extending from the branch of the right pulmonary artery into the cavity.

of this aneurysm which was responsible for the fatal hemorrhage.

CASE II. M. J. was a thirty-five year old foreign-born white woman whose husband had died from pulmonary tuberculosis one year before her admission. Her health was good, she maintained, until one month before coming to the sanitarium. Physical examination was essentially normal except for the chest which revealed dullness to percussion over the left lung and harsh breath sounds over both apices. X-ray film inspection revealed considerable involvement of the left lung and the sputum was positive for acid-fast bacilli. Her course was progressively downhill and she died six months after admission to the sanitarium with laryngeal and intestinal complications. Death, however, was sudden with massive pulmonary hemorrhage.

Pathologic examination of this lung (Fig. 4) revealed a 7 cm. cavity in the apex which was filled with a dark red blood clot. There was a smaller cavity measuring 2.5 cm. in diameter in the upper part of the lower lobe which was filled with what appeared to be an older clot and into this cavity protruded a 1.5 cm. aneurysmal dilatation of the pulmonary artery. Careful dissection revealed a rent in the wall of this aneurysmal dilatation which was the source of the bleeding.

CASE III. A. P., a thirty-five year old Negro woman, entered the sanitarium approximately six months after the onset of illness. She had been coughing and expectorating considerable material prior to admission and there was an occasional blood-streaked sputum. She was known to have had hypertension for some time and her blood pressure on admission was 195/120. Previously induced pneumothorax on the right obscured the physical findings but x-ray film revealed considerable disease in the right lung with most involvement apparently in the mid-lung field. In spite of supportive therapy her disease progressed and was complicated by severe tuberculous laryngitis. Approximately sixteen months after admission to the sanitarium she expired suddenly with massive pulmonary hemorrhage.

A middle section of the lungs showed a large cavity in the left lower lobe with a heavy fibrous wall surrounding it and pneumonic consolidation in the adjacent parenchyma. The remainder of the lungs showed a flooding of the acini with blood. (Fig. 5.) No residue of an earlier infection could be found and because of the nature of this lesion it was considered a young adult primary infection. Dissection failed to reveal any aneurysmal dilatation of a vessel; the source of hemorrhage was apparently the erosion of a branch of the pulmonary artery.

CASE IV. W. N. was a forty-three year old white man whose mother had died from pulmonary tuberculosis when he was seven years of age. He was in fairly good health until four years before admission, at which time he had a severe cold with a cough and pulmonary tuberculosis was diagnosed. He had been in and out of the sanitarium on numerous occasions, usually leaving against medical advice. Six months before final admission he suffered severe

FIG. 5. Close-up of the right lower lobe to show the flooding of acini with blood.

FIG. 6. Close-up of the larynx and upper portion of the trachea with a huge blood clot in place as was found at the time of postmortem examination.

pulmonary hemorrhage and continued to have blood-streaked sputum afterward. He was a known alcoholic and physical examination revealed a poorly nourished white male who showed evidence of marked weight loss (50 pounds) with physical findings of a markedly enlarged liver, dullness over the right lung field and many rales over the entire right lung and the mid-portion of the left lung. During his six months' stay in the sanitarium his lung picture did not change significantly but he had marked albuminuria, positive congo red test for amyloidosis, evidence of liver malfunction and sputum positive for acid-fast bacilli. He had a sudden massive pulmonary hemorrhage and expired.

Pathologically, there was a huge dark red blood clot projecting out of the larynx (Fig. 6) and on sectioning the lungs one saw that there was cavitation in both upper portions, that on the right being more extensive and most of the cavities were filled with dark red clotted blood. Extensive dissection failed to reveal the point of rupture of the pulmonary artery. The cyst-like cavities in the upper portion of the right lung communicated with bronchi and apparently represented old tuberculous cavities which had undergone "open-healing."

CASE V. S. F., a forty-three year old Negro man who was born in Memphis, Tennessee, had worked as a sand blaster for fourteen years. The onset of his illness was approximately one year before admission to the sanitarium. His chief complaint was weakness; there had been one episode of hemoptysis. Approximately two weeks after entering the sanitarium he suffered a massive fatal hemorrhage.

Sagittal sections revealed a large cavity in the right lung surrounded by consolidated parenchyma. Small firm nodulations were felt in portions of the lung. The left lung showed a cavity in the mid-portion and there were several caseous infiltrates noted in the lung parenchyma, especially in the upper portion. Smaller ulcerocaseous lesions were noted throughout the right lung. The lymph nodes were hard and rubbery in consistency and on section showed whorls of fibrous tissue indicative of some degree of silicosis. None of the cavities showed a definite limiting fibrous wall and careful dissection failed to reveal a bleeding point. This undoubtedly represents a case of

FIG. 7. Close-up to illustrate ulceration of a main bronchus; note the clot in place and the elliptic defect superior to it.

erosion of a vessel wall by one of these rapidly ulcerating lesions.

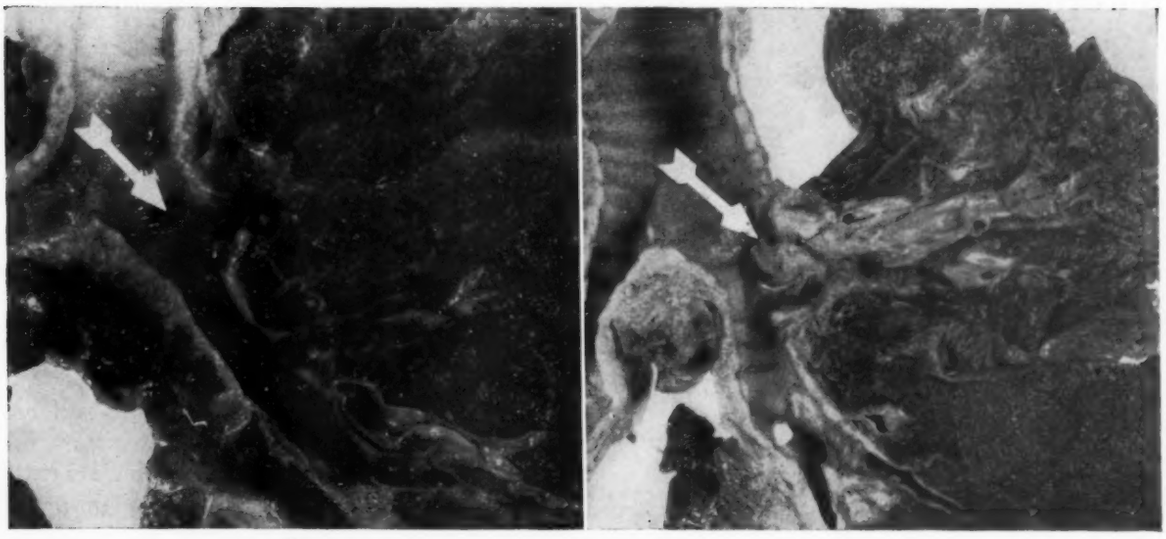
CASE VI. T. I., a sixty-one year old white foreign-born woman, was known to have pulmonary tuberculosis for at least nine years before admission to the sanitarium. During that time she had three or four acute febrile episodes but at no time did she require sanitarium care. Her husband had died from tuberculosis about six years before and x-ray films were taken periodically to determine the status of her pulmonary lesion. A febrile episode two months before admission was accompanied by high temperature, pain in the chest, cough, fatigue, and weight loss, and she expectorated a few cc. of yellowish sputum which was positive for acid-fast bacilli. Sanitarium care was recommended. Aside from a blood pressure of 170/100 physical findings upon admission were limited chiefly to the right lung which revealed slight dullness on percussion and limited excursions. No rales were heard in the chest at the time of admission. During her stay in the sanitarium she was given a course of streptomycin for approximately ninety days with some improvement. Bronchoscopy revealed a tuberculous endobronchitis on the right with bronchostenosis. Because of this finding right pneumonectomy was considered but she refused surgery. She was ambulatory for the most part during her stay in the sanitarium and occasionally showed some bloody streaking of the sputum. Approximately eighteen months after admission to the sanitarium she experienced a massive pulmonary hemorrhage.

A mid-section of the lung showed several fibrocaseous infiltrations scattered throughout the right lung with some fibrosis and retraction of the right apex. A rather large solitary fibrocaseous lesion was noted at the periphery of the right mid-lung field. There was marked ulceration of the mucosa of the mainstem bronchus and the secondary bronchi on the right. In the anterior portion of the lower lobe bronchus, a few centimeters from its origin, a large oval defect was noted. (Fig. 7.) This defect was almost entirely filled by an organized blood clot, however, there was a small elliptical opening superior to the clot through which a probe could be passed to communicate with the adjacent pulmonary artery. This case demonstrates well the erosion of a main vessel by a long-standing tuberculous endobronchitis.

CASE VII. M. P., a sixty-one year old white woman, foreign born, gave a history of having had the "flu" several times. For one year prior to admission she had slow progressive loss of weight and a few days before suffered a rather severe hemoptysis with streaking of the sputum every day thereafter. She entered a private hospital where a diagnosis of tuberculosis was made. Her sputum was positive for acid-fast bacilli and other laboratory examinations were negative with the exception of low grade hypochromic anemia. On bed rest over a period of six months she gradually improved but suddenly expired with a massive pulmonary hemorrhage.

At autopsy a defect was found in the left upper lobe bronchus. This defect measured 6 mm. in diameter and the base of it was formed by a firm peribronchial lymph node. (Fig. 8.) In the right main bronchus the mucosa was extremely thin and transparent and pigmented peribronchial nodes could be seen shining through. The hemorrhage arose from the bronchial artery which was eroded by the hard tuberculous node.

CASE VIII. H. Z., a twenty-six year old white man, was visiting friends in the city when he suffered a pulmonary hemorrhage and was admitted to the sanitarium as an emergency. He had never been treated in a tuberculosis sanitarium but he stated that at the age of two years he had whooping cough which necessitated hospitalization for twenty-four months. Subsequently, when he was admitted



8 9

FIG. 8. Close-up to show the black peribronchial node projecting through the anterior wall of the right main bronchus, and the clotted blood filling the lumen distally.

FIG. 9. Close-up showing the necrotic lesion and the slightly enlarged hilar lymph node. The node contained some small caseous infiltrations.

to grammar school a chest x-ray film was taken and his parents were informed that there was considerable scarring of his lungs compatible with healed tuberculosis. In the years following he was hospitalized frequently because of his "weakened" condition. He stated that recently he had developed slight cough with a very small amount of expectoration, experienced some chest pain and had mild dyspnea on exertion. Occasionally there were evening temperature elevations up to 101°F.

Physical examination revealed a well developed and well nourished white man apprehensive and acutely ill. Examination of the chest showed impaired resonance and bronchial breathing over the right base. Sputum specimen was negative for acid-fast bacilli. Three days after admission to the sanitarium he suffered a severe pulmonary hemorrhage and expired.

A mid-section of the lung disclosed a few small fibrocaseous tubercles in the upper portion of each lung. These tubercles appeared to be fairly well encapsulated. At a point in the right bronchus where the upper lobe bronchus takes its origin there was a necrotic area approximately 1.0 cm. in diameter (Fig. 9) and a section of this lesion revealed that the entire bronchial wall was involved in this necrotizing process. This lesion eroded a branch of the bronchial artery and was responsible for the massive hemorrhage that was seen. The parenchymal disease was quiescent.

COMMENTS

Probably a massive hemorrhage produces death by suffocation, although in some instances, the loss of blood itself may be sufficient to terminate a cachectic individual. An estimation of the actual blood loss is difficult, as one must consider the amount of blood coughed up and expelled and that found in the lung and gastrointestinal tract at the time of postmortem examination. There is not much doubt that, in some cases, the total volume approximates 1,000 cc. Most patients die suddenly following a massive hemorrhage, and do not present the picture of exsanguination. The amount of blood necessary to produce death by suffocation probably varies greatly and is dependent upon several factors. When the main airways are filled to overflowing (as seen in Figure 6) undoubtedly the individual is asphyxiated by his own blood. On the other hand, collections of blood in the functional parenchyma in a lung partially destroyed by a previous disease (as seen in Figure 5) and with limited reserve may likewise asphyxiate an individual even though the volume of blood is not so great.

The presence of a definite aneurysm has been

the exception instead of the rule in the routine examination of lungs from fatal hemorrhage cases at this institution. It was impossible to identify the bleeding vessel in many cases; however, this is true in instances of hemorrhage from other organ systems. A compilation of the findings in eighty consecutive cases is listed below:

Bleeding Point	No. of Cases
None identified	61
Pulmonary artery (no aneurysm)	8
Rasmussen aneurysm	6
Bronchial artery	5
Total	80

Even though the caliber of the involved vessels varied considerably in different cases no correlation could be made between the size of the vessel and the magnitude of the hemorrhage or the rapidity of death. Profuse hemorrhage from the small bronchial arteries correspond to hemorrhages from the larger pulmonary artery branches because of the differences in pressure. The pressure in the lesser (pulmonary) circulation is estimated to be about one-sixth (mean value) that of the greater (systemic) circulation. Since the bronchial artery is derived from the aorta, the pressure no doubt is consistent with systemic pressure. When the lung has widespread involvement, the amount of blood flowing through the pulmonary arteries to the affected parts is proportionately reduced and the pressure is correspondingly less. Recent work by Marchand et al.[5] has shown that the pattern of the bronchial arteries varies considerably in disease; however, the pressure within the vessels probably is not altered to any appreciable degree. In the two instances (Cases VII and VIII) in which the bronchial artery was the source of bleeding, the lesion was located near the main trunk of the vessels. Whether the smaller ramifications of the vessel are ever involved is questionable; it is our belief that a branch of the pulmonary artery is the most likely source of hemorrhage at any point in the lung distal to the secondary bronchi.

The cases presented emphasize the multiplicity of mechanisms involved in fatal massive hemorrhage. It is true that many cases show a ruptured Rasmussen's aneurysm (and the incidence of this lesion varies with different institutions) but the majority reveal only an erosion of a branch of the pulmonary artery without any significant aneurysmal dilatation.

SUMMARY

A survey of 2,830 autopsies at Municipal Tuberculosis Sanitarium, Chicago, was made and a report of 138 patients whose deaths were attributable to pulmonary hemorrhage were analyzed. Selective cases were described in detail to illustrate the different mechanisms of massive hemorrhage and a review of the literature given.

REFERENCES

1. Codina Suque, J. and Mansilla Delicado, R. F. Consideraciones sobre un caso de hemoptisis mortal. *Rev. clin. espan̄.*, 3: 528, 1941.
2. Goldberg, B. Clinical Tuberculosis. The Pathology of Pulmonary Tuberculosis by R. H. Jaffe, 5th ed., vol. 1, pp. A105–A157. Philadelphia, 1946. F. A. Davis Co.
3. Klosk, E. Unusual form of fatal hemorrhage in course of chronic pulmonary tuberculosis clinically arrested, *Quart. Bull. Sea View Hosp.*, 3: 176, 1938.
4. Lopez, Q. M. Las hemoptisis terminales en la tuberculosis del adulto. *Semana méd.*, 1: 877, 1946.
5. Marchand, P., Gilroy, J. C. and Wilson, V. H. Anatomical study of bronchial vascular system and its variations in disease, *Thorax*, 5: 207, 1950.
6. O'Leary, C. Death from haemoptysis occurring in infant of nine months, *Tubercle*, 19: 513, 1930.
7. Petersen, W. F. The Patient and the Weather, vol. 4, pt. 2, pp. 663–670. Ann Arbor, Mich., 1937. Edwards Brothers Inc.
8. Plessinger, V. A. and Jolly, P. N. Rasmussen's aneurysms and fatal hemorrhage in pulmonary tuberculosis. *Am. Rev. Tuberc.*, 60: 589, 1949.
9. Rasmussen, V. Hemoptysis, especially when fatal, in its anatomical and clinical aspects. Translated by W. D. Moore. *Edinburgh M. J.*, 14: 385, 1868.

Indications for Treatment of Tuberculosis in Children*

EDITH M. LINCOLN, M.D., *New York, New York*

From the Department of Pediatrics, New York University College of Medicine, and the Chest Clinic of the Children's Medical Service, Bellevue Hospital, New York, N. Y.

EVERY form of tuberculosis may be seen in children. However, the great majority of clinical pictures are manifestations of primary or first infection pulmonary tuberculosis and are due to local progression of the disease at the portal of entry or to complications due to metastasis through the lymphohematogenous route. Chronic pulmonary tuberculosis, often called reinfection tuberculosis, occurs much more rarely in the child than in the adult. Moreover, the clinical course and the treatment of chronic pulmonary tuberculosis is essentially the same at all ages. Therefore, this presentation will be limited to a discussion of the indications for treatment of primary tuberculosis and of the many complications which constitute its clinical picture.[1]

GENERAL MANAGEMENT OF THE TUBERCULOUS CHILD

Every child with active primary tuberculosis, regardless of the presence or absence of symptoms, is entitled to excellent general care and supervision. A child with uncomplicated primary tuberculosis need not be treated in a hospital or sanatorium unless his home is inadequate for his care or the source case remains in the home. Limitation of activity is desirable during the early months of the disease even if the child is afebrile. The child need not be kept in bed nor indoors, but play must be supervised and toys selected to minimize excitement and overactivity. Children of school age who are past the acute stage of the disease may attend school if afebrile and provided physical activities can be restricted. Excessive exposure to sunlight should be avoided, and the child with active tuberculosis should be shielded from measles and given gamma globulin if exposed. Diet should be liberal in calories and in foods high in protein and fat, and supplementary vitamins should be given.

The degree and duration of conservative treatment will vary with the extent of tuberculous disease but, in general, activity is increased gradually after six months have passed and most restrictions are lifted after a year since most observers agree that more than 90 per cent of serious complications occur within the first year after the diagnosis of primary tuberculosis.

SELECTION OF CASES FOR SPECIFIC THERAPY

The selection of patients who need specific antimicrobial therapy in addition to conservative treatment is based largely on the estimated prognosis of each individual patient. It is obviously mandatory to treat patients with forms of tuberculosis who had a high death rate prior to the use of specific therapy. Meningitis and miliary tuberculosis, which were practically 100 per cent fatal before chemotherapy, must of course be treated. In addition there are two other main causes of death in tuberculous children for which treatment is essential: (1) locally progressive primary pulmonary tuberculosis with cavitation and bronchogenic spread, and (2) various forms of hematogenous tuberculosis more protracted than miliary in which multiple foci of tuberculosis are produced by blood stream invasion.[2] Such forms of tuberculosis must be treated as a lifesaving measure. In untreated meningitis the average duration from first symptom to death was only nineteen and a half days. Therefore, once the diagnosis of meningitis is established it is important to give the most efficient antimicrobial agents, streptomycin and isoniazid together and in maximum dosage, changing

* This study was aided by grants from the committee on Medical Research of the American Trudeau Society, medical section of the National Tuberculosis Association; from the Division of Research Grants and Fellowships of the National Institutes of Health, Public Health Service; from Parke, Davis and Company.

the dosage to a level less likely to cause toxicity when the patient seems to be making a clinical recovery and when the sugar content in the cerebrospinal fluid is returning to a normal level. Treatment should be continued for at least a year. Many schemes of therapy of tuberculous meningitis have been reported and there is certainly no one method that invariably cures the disease.[3,4] The essentials for success are early diagnosis, prompt and vigorous therapy, and prolonged treatment.*

Most clinicians treat miliary tuberculosis as intensively as meningitis, because of the previous high mortality rate, using both streptomycin and isoniazid and reducing the dosage only after definite clinical and roentgen improvement. However, excellent results have been reported without the use of streptomycin.[5]

In miliary tuberculosis it is important that isoniazid be continued, although not in maximum dosage, for a year in an effort to prevent the development of meningitis.

Except in meningitis and miliary tuberculosis it seems neither necessary nor wise to treat tuberculosis with a combination of the two most effective antimicrobial agents. Tuberculosis is by nature a chronic disease and it would seem better whenever possible to reserve one potent antituberculous agent for possible later use. It must be borne in mind that no drug known at present effects a complete cure. The object of therapy is not eradication of the disease but the achievement of bacteriostasis sufficient to supplement the patient's natural resistance to tuberculosis.

Because of its minimal toxic side effects and ease of administration, isoniazid rather than streptomycin is often used in the therapy of protracted hematogenous tuberculosis and locally progressive primary tuberculosis. It

Outline of Specific Therapy*

CHEST CLINIC OF THE CHILDREN'S MEDICAL SERVICE OF BELLEVUE HOSPITAL (NOVEMBER, 1954)

Tuberculous Meningitis		
Streptomycin:	Intramuscular for 6 months	× 1.0 gm. daily for minimum period of 1 month or until cerebrospinal fluid sugar has been normal for 1 week; thereafter b.i.w.
Isoniazid:	Oral for 6–12 months	× 10 mg./Kg. daily for 4 to 6 weeks; thereafter 7 mg./Kg.
Promizole:	Oral for 2 years	× 0.25 to 8.0 gm. daily
Miliary Tuberculosis		
Isoniazid:	Oral for 1 year	× 10 mg./Kg. daily for 4 to 6 weeks; thereafter 7 mg./Kg.
Promizole:	Oral for 2 years	× 0.25 to 8 gm. daily
Streptomycin:	Intramuscular for 4 months	× 1.0 gm. daily; later b.i.w.; in some cases streptomycin is omitted
Relapse: Repeat original course of therapy.		

In other forms of tuberculosis which require therapy, isoniazid is given daily in doses of 5 mg./Kg., with daily PAS or promizole; or streptomycin is given daily or b.i.w. on weight basis combined with daily PAS or promizole. Streptomycin and isoniazid are rarely given together except as a lifesaving measure. Therapy is frequently prolonged for a year or more.

Dosage Schedule for Streptomycin (weight basis)

0.3 gm.—under 10 lb.
0.4 gm.—10 through 19 lb.
0.5 gm.—20 through 39 lb.
0.6 gm.—40 through 59 lb.
0.75 gm.—60 through 89 lb.
1.0 gm.—90 lb. and over

Isoniazid:	Given by mouth every 12 hours. In case of vomiting same amount may be given intramuscularly.
Promizole:	Given by mouth every 6 hours. In absence of signs of toxicity a gradual step-like increase from 0.5 gm. is made every few days until a blood level of 1–3 mg. per cent is obtained (taken 2½–3 hours after a dose of promizole).
PAS:	Para-aminosalicylic acid. Given by mouth every 4 hours for 3 or 4 daily doses, 0.5 gm./Kg./24 hours up to maximum of 12 gm. daily dose.
Streptomycin:	A 1.0 gm. daily dose is sometimes divided in two for comfort of the patient. Smaller doses are given as single daily injections except in small or emaciated patients.

* Subject to modification for individual cases.

* An outline of specific therapy of tuberculosis in use in the Chest Clinic of the Children's Medical Service of Bellevue Hospital is appended for those who wish suggestions for more detailed schemes of treatment.

need not be given in maximum dosage except in patients with fulminating disease. Treatment should always be prolonged for at least a year and longer if necessary, until three to six months after the disease is apparently controlled and signs and symptoms have disappeared. In cavitating primary tuberculosis the disease is considered under control when cultures from gastric washings have been negative, cavities have been closed and roentgenograms stabilized for a period of six months. If these objectives cannot be reached, surgical removal of the residual disease should always be considered while the patient is still receiving antimicrobial therapy. The duration of specific therapy after surgery is usually dependent on the pathologic findings in the resected specimen.

If streptomycin is used in the treatment of these complications, it should always be used in combination with a secondary drug, such as PAS (para-aminosalicylic acid) or promizole® because the emergence of resistant organisms may be delayed by this method and the value of each drug enhanced by their combined use. Most physicians prefer to use isoniazid also in combined therapy in the same manner, but excellent investigators advocate the use of isoniazid alone.[5]

Formerly two of three children with protracted hematogenous tuberculosis or cavitating primary tuberculosis died of tuberculosis. With specific therapy practically all survive. However, it may be wise to emphasize that just as in tuberculous meningitis, prompt diagnosis and consistent prolonged therapy results not only in a better survival rate but also in less residual disease in the survivors.

In addition to the patients in whom specific treatment is indicated to save life, antimicrobial treatment may be useful in alleviating symptoms or in shortening the course of the disease. With treatment most forms of tuberculosis of the skin will heal rapidly and draining cutaneous sinuses close promptly, thus often permitting surgery of the underlying tuberculous disease in bones or nodes. The potential danger of dissemination following surgery can be minimized by protecting the tuberculous patient with antimicrobial therapy during a surgical procedure and for a short time thereafter. Specific therapy will usually give rapid relief from harassing symptoms in the uncommon cases of tuberculosis of the gastrointestinal and genitourinary tracts in children, as well as frequently producing roentgen evidence of anatomic healing. In these forms of tuberculosis in which antimicrobial therapy is not used as a lifesaving measure the two major drugs, isoniazid and streptomycin, should not be used in combination. One should be saved for possible later use, and the drug selected should be used in effective, but not maximum dosage.

In a large group of complications of primary tuberculosis, examples of which are tuberculosis of the bones and nodes, great chronicity is often exhibited with periods of spontaneous remission even when no specific therapy is used. In such cases the indications for therapy are never sharply defined and it is difficult to evaluate the results of treatment. Nevertheless, attempts at specific therapy are always justified provided isoniazid and streptomycin are not employed together and toxicity from either drug is avoided.

In still another group of complications of primary tuberculosis there is no apparent response to antimicrobial therapy and therefore no clear indication for specific treatment. For example, in endobronchial tuberculosis caused by caseous nodes encroaching on the bronchi, neither the symptoms nor the appearance on bronchoscopy shows an apparent response to therapy.[6] Progression of the disease has been repeatedly observed while the patient is receiving antimicrobial therapy. Therefore, the presence of endobronchial tuberculosis caused by primary tuberculosis does not constitute a clear indication for specific therapy. In many cases the lesion will undoubtedly heal as well without therapy. However, in infants with severe symptoms or whenever bronchogenic dissemination seems likely to occur, the use of antimicrobial therapy would seem to be indicated to control the spread of the disease rather than to treat the local condition.

When streptomycin was the only very effective antimicrobial agent, asymptomatic primary tuberculosis was also included in the group of cases in which therapy was not clearly indicated. The use of streptomycin did not prevent complications, a notable example being the development of meningitis in children under treatment for miliary tuberculosis. Moreover, evidence of local response of the primary complex was not obtained. The addition of isoniazid to the list of antimicrobial agents may change the indications for the treatment of asymptomatic primary pulmonary

tuberculosis. There is as yet no definite evidence that isoniazid hastens the resolution of the primary complex. However, there is evidence that clinical meningitis does not develop in children, even in those with miliary tuberculosis, who are receiving adequate treatment with isoniazid. Studies of carefully controlled series of children with primary tuberculosis, in which the patients to be treated are selected at random, are needed to prove the effectiveness of isoniazid in the prevention of meningitis as well as the proper dosage and necessary duration of therapy. Such studies are now in progress and the results will determine whether treatment with isoniazid will be indicated in every child with roentgen evidence of primary tuberculosis, even if the child is free from symptoms.

Antimicrobial therapy has already had a marked beneficial effect on the prognosis of primary tuberculosis in children.[7] On the children's tuberculosis ward of Bellevue Hospital the death rate from 1930 through 1946 was 21.5 per cent; after the introduction of streptomycin the mortality was only 5 per cent annually. Following the addition of isoniazid the rate fell to 1.5 per cent. The prognosis of primary tuberculosis will be improved still further if it can be proved that meningitis and other major complications can be prevented by treating a child with primary tuberculosis.

It is obvious that the indications for the use of antimicrobial therapy vary greatly in different forms of primary tuberculosis in children. In some complications the use of specific treatment is mandatory as a lifesaving measure; in others it is highly recommended because it alleviates symptoms, may limit or prevent crippling effects or produce anatomic healing. In still other complications the indications for therapy are not clear because of the ill-defined responses obtained. Finally there is accumulating evidence that at some time in the future the mere diagnosis of active primary pulmonary tuberculosis, even in an asymptomatic child, may constitute an indication for treatment with isoniazid.

REFERENCES

1. Lincoln, E. M., Sewell, E. M. and Anastasiades, A. A. The treatment of primary tuberculosis in children. *Postgrad. Med.*, 16: 422, 1954.
2. Lincoln, E. M. Hematogenous tuberculosis in children. *Am. J. Dis. Child.*, 50: 84–103, 1935.
3. Debré, R. The prognosis of tuberculous meningitis. *Am. Rev. Tuberc.*, 65: 168, 1952.
4. Lincoln, E. M. and Sifontes, J. E. Tuberculous meningitis in children. *M. Clin. North America*, 37: 345–362, 1953.
5. Deuschle, K., Ormond, L., Elmendorf, D., Jr., Muschenheim, C. and McDermott, W. The course of pulmonary tuberculosis during long-term, single drug (isoniazid) therapy. *Am. Rev. Tuberc.*, 70: 228–257, 1954.
6. Daly, J. F., Brown, D. S., Lincoln, E. M. and Wilking, V. N. Endobronchial tuberculosis in children. *Dis. of Chest*, 22: 380, 1952.
7. Lincoln, E. M. Course and prognosis of tuberculosis in children. *J. A. M. A.*, 9: 623–632, 1950.

The Role of Resection for Pulmonary Tuberculosis in Children and Adolescents

MORRIS RUBIN, M.D., *New York, New York*

IN less than a decade a radical change has taken place in the treatment of pulmonary tuberculosis. The sanatorium "rest cure" no longer occupies its time-honored position. Bed-rest is now used as an adjunct to more direct and definitive measures and for comparatively short periods of time. It is becoming so difficult to find the requisite indications for inducing pneumothorax that this treatment is rapidly being abandoned in many institutions. The recent popularity of therapeutic pneumoperitoneum as a "holding"-type of treatment is on the wane. Extrapleural thoracoplasty, once the mainstay in surgical treatment, is now used to a limited degree.

The current treatment of pulmonary tuberculosis centers around specific antituberculosis agents (streptomycin, dihydrostreptomycin, para-aminosalicylic acid and isoniazid) in combination with resection when indicated. The latter is utilized not only for cavitary disease or for a smoldering focus discharging acid-fast bacilli, but also for relatively circumscribed disease, temporarily under control, but which may be a hazard to the individual upon his resumption of normal activities.

The place of resectional surgery in the treatment of pulmonary tuberculosis, as outlined, is being applied almost exclusively to adults. In children and adolescents it is practically an unexplored field for several reasons. First, there are few institutions which admit and provide prolonged care for children with tuberculosis. Second, the belief is widely held that tuberculosis in younger age groups behaves in extremes: that the disease represents a primary infection and is either innocuous in the vast majority, or else is an acute generalized infection leading to a fatal issue. Although the recent introduction of antituberculosis drugs has modified medical opinion as to the dire prognosis associated with hematogenous tuberculosis, the basic concepts of the evolution of the disease have remained unchanged. Few physicians realize that in a certain proportion of children, pulmonary tuberculosis behaves much in the same manner as it does in adults and that in these a sharp distinction between so-called childhood and adult types of tuberculosis is not valid.

Shortly following the introduction of specific antituberculosis agents, which help to bring about a resolution of the exudative component of the tuberculous process, the need arose of treating children with residual caseous foci or permanently damaged lung tissue. It was decided to apply resectional treatment as was being employed in adults. This plan was adopted in 1949 and a preliminary report on thirty children and adolescents was published in 1952.[1] The initial results, based on a six-month to a three-year follow-up, warranted the conclusion that resection had a definite place in the treatment of pulmonary tuberculosis in children. Since then a total of sixty-two children and teenagers have been treated in this manner. In addition to determining the place of resectional surgery in children, this study afforded an unusual opportunity of correlating the various clinical-pathologic patterns of tuberculosis.

CLINICAL DATA

As shown in Table I there were fifty-three females and nine males, the majority Negro and Puerto Rican girls. The known duration of illness prior to surgery is shown in Table II. As noted, a considerable number had been hospitalized for two years or longer, some on repeated occasions. A few selected cases were operated upon within six months of the onset of their illness. The timing of resection was based largely on the course of the disease as seen in sequential chest x-rays. When a patient failed to improve, resection came into consideration. The operative procedures performed are shown in Table III. It should be noted that

limited resections were possible in forty-seven and pneumonectomy in only eleven.

The various types of lesions resected are shown in Table IV. The material lent itself to a division of two major groupings: (1) the primary infection, encountered almost exclusively in children under ten years of age and (2) tuberculosis in the adolescent, which was more apt to resemble tuberculosis in the adult. Each group was found to possess distinctive clinical, roentgenologic and morphologic features presenting different problems in treatment. Table IV is a composite of certain clinical and morphologic characteristics which typified the several subgroups. The table is not to be construed as a classification of tuberculosis in the strict sense of the term, rather as types of disease which may present indications for resection.

TABLE I
DISTRIBUTION OF DISEASE

Age (Onset of Disease)	Number
2 to 5 yr.	3
6 to 10 yr.	10
11 to 15 yr.	31
16 to 19 yr.	18
Race	
Negro	33
Puerto Rican	15
White	14
Sex	
Females	53
Males	9

TABLE II
KNOWN DURATION OF ILLNESS PRIOR TO SURGERY

Months	No. of Patients
2– 6	8
7–12	25
13–18	12
19–24	5
25–30	3
31–36	5
37–42	1
4 yr.	2
5 yr.	1

TABLE III
OPERATIVE PROCEDURES

Procedure	No. of Patients
Segmental resections (8):	
Apicopost. (L.U.L.)	6
Lateral (R.M.L.)	2
Lobectomies (39):	
R.U.L.	14
R.U.L. and R.M.L.	1
R.M.L. and R.L.L.	2
R.M.L.	3
R.L.L.	5
L.U.L.	10
L.U.L. and sup. seg. L.L.L.	2
L.L.L. with seg. L.U.L.	1
L.L.L. and R.U.L.	1
Pneumonectomies (11):	
Right	6
Left	5
Attempted resections (4):	
Resection not performed due to extent of disease	2
Cardiac arrest	1
Frozen hilum due to lymph nodes	1

TABLE IV
TYPES OF TUBERCULOUS LESIONS RESECTED

Primary tuberculosis:
1. Large, stationary caseous focus
2. Primary cavity
3. Persistent atelectasis
   (a) Segmental
   (b) Lobar: shrunken middle lobe
4. Postprimary bronchiectasis
5. Bronchostenosis: destroyed lung

Tuberculosis in the adolescent:
6. Caseonecrotic foci
   (a) Solitary
   (b) Confluent nodular
7. Caseocavitary tuberculosis
8. Tuberculosis of small bronchi
9. Bronchiectasis: destroyed lobe
10. "Minimal" lesion

PRIMARY TUBERCULOSIS

Large Stationary Caseous Focus

CASE 1. P. W., a three year old Negro boy whose mother had tuberculosis, was admitted to Seton Hospital on December 29, 1951, with tuberculosis of the right middle lobe, discovered in a routine chest x-ray. (Fig. 1A.) Gastric cultures were repeatedly positive for acid-fast bacilli prior to antibiotic therapy. He was given streptomycin and later isoniazid with considerable resolution of the lesion. A large round focus persisted in the lateral segment of the middle lobe. (Fig. 1B, C.) On December 17, 1952, fifteen months after the discovery of the lesion, the lateral segment of the middle lobe was resected. At operation numerous filmy adhesions were encountered between lung and chest wall.

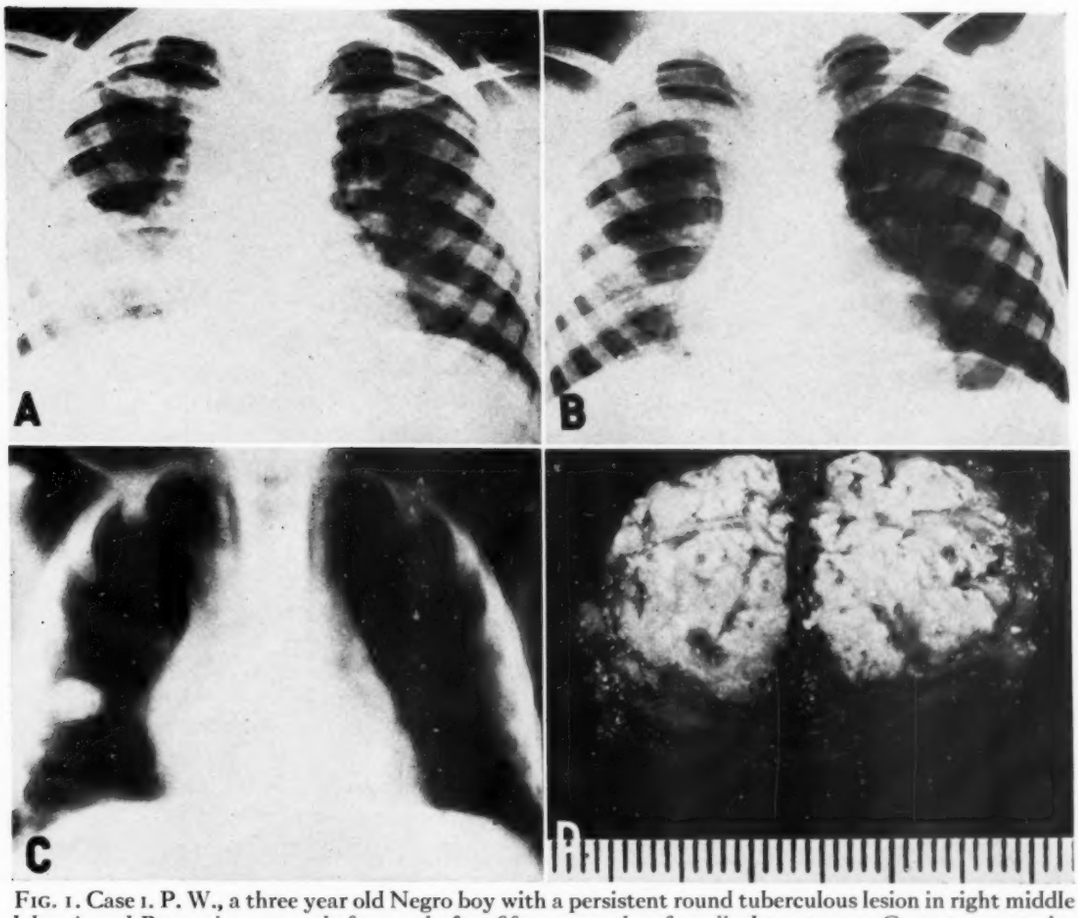


FIG. 1. Case 1. P. W., a three year old Negro boy with a persistent round tuberculous lesion in right middle lobe. A and B, routine x-rays before and after fifteen months of medical treatment. C, postero-anterior tomogram showing large round mass in lateral segment of middle lobe. D, resected lateral segment consists of atelectatic lung surrounding a large caseous focus.

The lateral segment of the middle lobe was atelectatic and contained a hard, round mass about the size of a hazelnut. The hilar nodes were enlarged. The child made an uneventful recovery and has remained well. Gross examination of the specimen showed the segment of lung occupied for the most part by a firm, rounded, well defined caseous focus, measuring 3 by 2.5 cm. (Fig. 1D.) It was not encapsulated, was compressing, but did not involve the adjacent bronchi. On microscopic examination the mass was composed of caseous material, surrounded by a thin rim of fibrous tissue. It was subdivided by thin fibrous bands into smaller caseous foci many of which contained deposits of calcium. Occasional tubercles were seen in the mucosa of the larger bronchi.

Comment. The indication for resecting this type of primary tuberculosis presented itself in only two cases. The caseous focus in this patient undoubtedly represented a primary lesion. It was excised because of its large dimension after fifteen months of treatment.

Primary Cavity

CASE 11. C. S., a seven year old white girl developed a respiratory infection in October, 1951. A chest x-ray revealed a collapsed right upper lobe. (Fig. 2A.) A large round mass within this area of density was interpreted as a calcified paratracheal lymph node. (Fig. 2B) Admission gastric cultures were positive for acid-fast bacilli. A bronchoscopy on May 2, 1952, revealed no gross involvement of the major bronchi. The patient received a course of streptomycin without any change in the radiographic appearance of the lesion. On May 8, 1952, right upper lobe lobectomy was performed. At operation a shrunken and fibrotic lobe was found which contained a hard round mass about the size of a walnut. This mass had simulated the enlarged paratracheal node

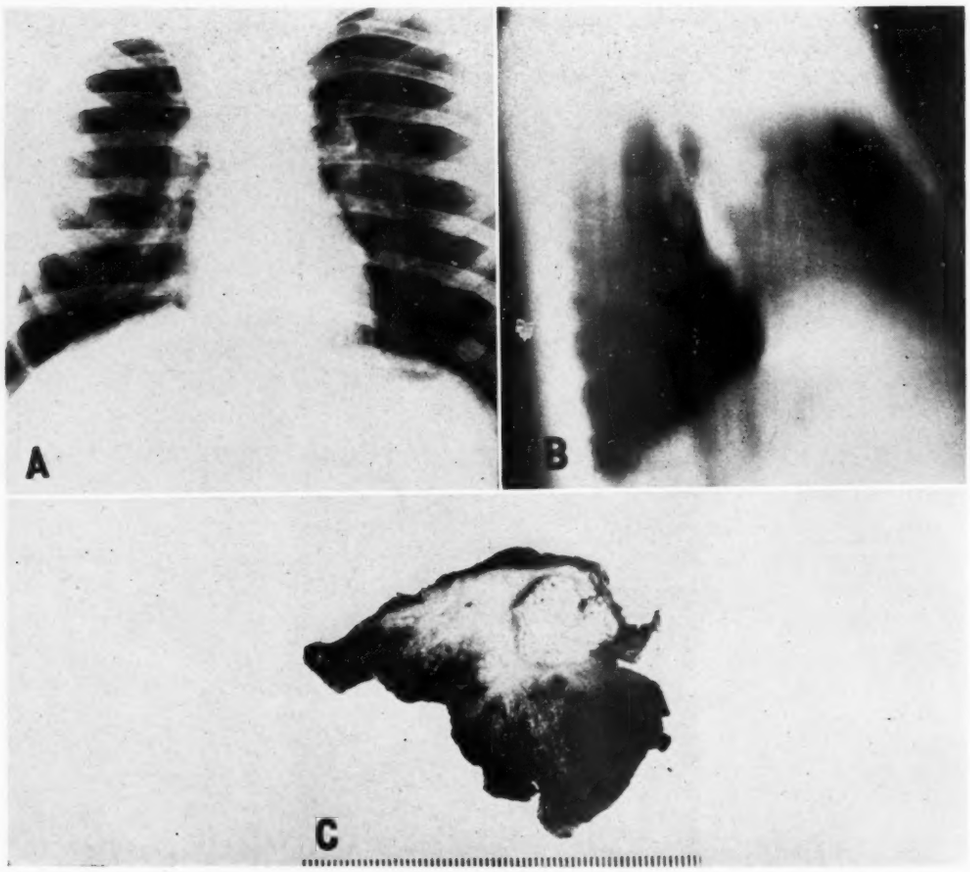


FIG. 2. Case II. C. S., a seven year old white girl with a chronic respiratory infection. Gastric cultures were positive for acid-fast bacilli. A, x-ray of chest on admission revealed a shrunken right upper lobe. B, lateral tomogram shows a rounded mass interpreted as a paratracheal lymph node. C, the resected lobe is shrunken and fibrotic with a cavitated primary caseous focus, simulating a tuberculous lymph node.

mentioned previously. No difficulty was encountered in the hilar dissection. The patient was discharged after an uneventful convalescence. She is well and attending school. The specimen consisted of a shrunken lobe with thickened visceral pleura which, on cut section, revealed a large caseous mass with a central cavity about the size of a dime. (Fig. 2C.) The cavity was filled with necrotic caseous material. The lobe was markedly fibrotic with thickened, distorted bronchi. On microscopic examination the wall of the cavity was composed of very cellular fibrous tissue. There was destruction of an adjacent bronchus by tuberculous granulation tissue.

Comment. Resection was performed in this case for a persistently shrunken lobe with occasionally positive gastric cultures. The caseocavitary lesion probably represented a primary focus. The degree of fibrosis within the lobe indicated disease of longer duration than the history indicated.

Persistent Segmental Atelectasis

CASE III. J. R., a four year old Puerto Rican boy, was admitted to Seton Hospital on March 24, 1952, with a history of cough of six months' duration. A chest x-ray taken on admission revealed an extensive consolidation of the left upper lobe. (Fig. 3A.) Additional x-rays, including tomography, suggested areas of cavitation within this area. There was widening of the mediastinum due to enlarged lymph nodes. One gastric culture was positive for acid-fast bacilli. In June, 1952, streptomycin was started and given for a total of 44 gm. Isoniazid was added in October, 1952. Serial chest x-rays over a period of one year showed considerable diminution in the size of the lesion. (Fig. 3B.) Bronchoscopy on

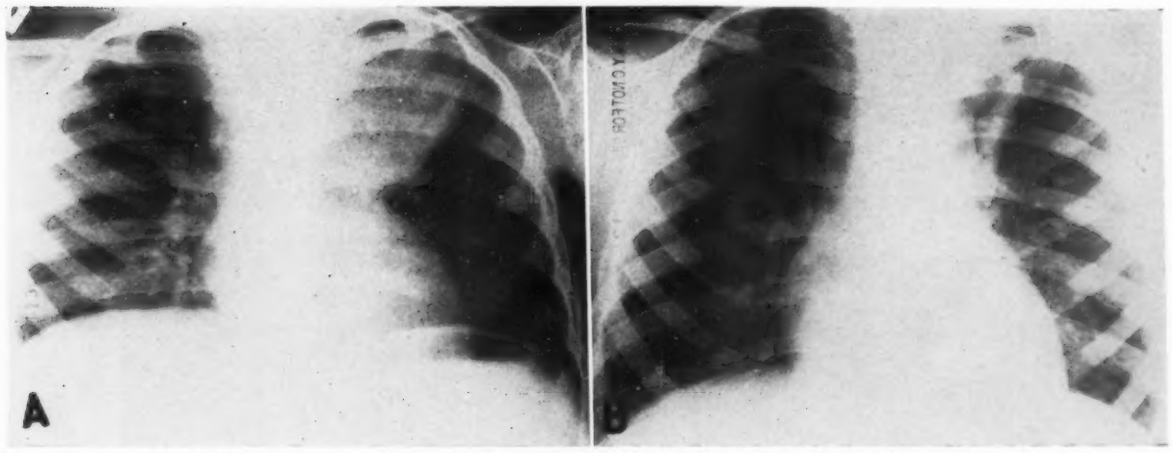


FIG. 3. Case III. J. R., a four year old Puerto Rican boy with a six-month history of illness prior to admission to the hospital. Gastric cultures on admission were positive for acid-fast bacilli. A, routine x-ray before treatment showing extensive consolidation of the left upper lobe. B, x-ray of chest after twelve months' medical therapy showing residual disease in the left upper lobe. At operation an area of segmental collapse was encountered.

February 27, 1953, revealed no endobronchial disease. An area of density persisted in the left upper lobe, the nature of which could not be determined. The child was explored on March 26, 1953, one year after admission. Considerable hilar induration was encountered due to enlarged lymph nodes. The left upper lobe contained an area of atelectasis in the anterior segment which, on palpation, contained numerous small nodules. Similar nodules could also be felt in the lingula and in the apex of the left lower lobe. The atelectatic area alone was excised over clamps. The postoperative course was uneventful. The child has remained well since discharge. The specimen consisted of a shrunken segment of lung which, on microscopic examination, showed focal atelectasis. Peribronchial tubercles were noted throughout the specimen.

Comment. It was difficult from the clinical and bizarre radiographic findings to determine the nature of the residual area of consolidation in the left upper lobe. The atelectatic segment was probably an area of "absorption-collapse," so-called epituberculosis, which in this case could not be differentiated from caseocavernous tuberculosis.

Lobar Atelectasis: Shrunken Middle Lobe

CASE IV. M. B., a ten year old Negro girl, developed a cough one month prior to admission to Seton Hospital. A chest x-ray showed involvement of the right middle lobe. (Fig. 4A and B.) Sputum and gastric cultures were persistently negative for acid-fast bacilli. Bronchoscopy in February, 1953 showed redness and swelling of the mucosa around the orifice of the middle lobe bronchus. The patient was treated with streptomycin from November, 1952 to April, 1953. Although there was considerable improvement radiographically, atelectasis of the lateral segment persisted after fifteen months' observation. (Fig. 4C.) On December 17, 1953, the right middle lobe was resected. Except for a portion of the medial segment which was aerated, the lobe was shrunken and nodular. Hilar induration required excision of the lobe by the clamp technic. The patient's postoperative course was uneventful. She is well and attending school. Pathologic examination of the shrunken lobe disclosed two large caseous lymph nodes encircling and compressing the middle lobe bronchus. Within the parenchyma there were irregular caseous foci. (Fig. 4D.) Microscopically, the caseous masses were surrounded by a broad rim of very vascular and cellular tuberculous granulation tissue which, in turn, was surrounded by atelectatic lung parenchyma.

Comment. The indication for resecting the middle lobe was the persistent atelectasis. It was surprising how much caseous disease the lobe contained.

Postprimary Bronchiectasis

CASE V. L. K., an eleven year old Negro girl, was found to have a density in the right upper lobe in a chest x-ray taken after her mother's death from tuberculosis. The patient was treated in another hospital for eleven

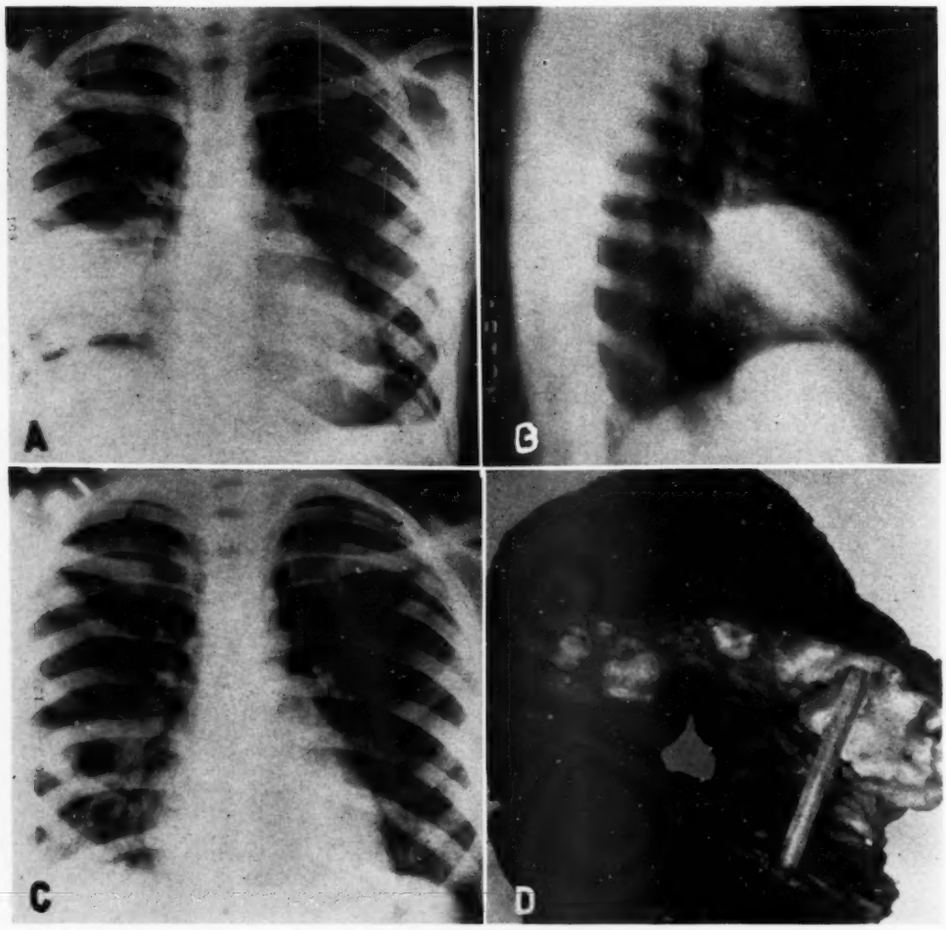


FIG. 4. Case IV. M. B., a ten year old Negro girl with tuberculosis of the right middle lobe. A and B, admission x-rays showing consolidated middle lobe. C, residual disease present after fifteen months' medical treatment. D, specimen shows caseous tuberculosis of the lobe and hilar lymph nodes.

months before her admission to Seton Hospital. Gastric cultures were occasionally positive for acid-fast bacilli. X-ray of the chest revealed an oval density in the right upper lobe which, in the lateral view, could be localized to the anterior segment. (Fig. 5A.) The patient was given a course of streptomycin. In April, 1949, abdominal pain, fever and distention developed which was diagnosed as tuberculous peritonitis. The symptoms subsided after another course of streptomycin. In August, 1949, fever again developed and the patient was found to have left pleural effusion which cleared spontaneously in a few months. Bronchoscopy on March 12, 1951, showed edema around the orifice of the right upper lobe bronchus. Serial chest x-rays revealed a shrunken anterior segment of the right upper lobe. (Fig. 5B.) Sputum cultures continued to show acid-fast bacilli. On April 4, 1951, right upper lobe lobectomy was performed. At operation an atelectatic anterior segment was found which, on palpation, was firm and nodular. The apical and posterior segments appeared uninvolved. The patient made an uneventful recovery and has been well since her operation. (Fig. 5C.) The specimen showed partial compression of the lobar bronchus by a hard lymph node. The anterior segmental bronchus was completely occluded by a dense scar. Distal to this scar the bronchi were dilated, and the lung parenchyma atelectatic. (Fig. 5D.) On microscopic section tubercles were noted in the mucosa and submucosa of the involved bronchi.

Comment. The indications for resection were the positive gastric cultures and the persistent bronchiectasis. The involved hilar node and the dense scar within the anterior segment of the lobe probably represented a healed primary complex.

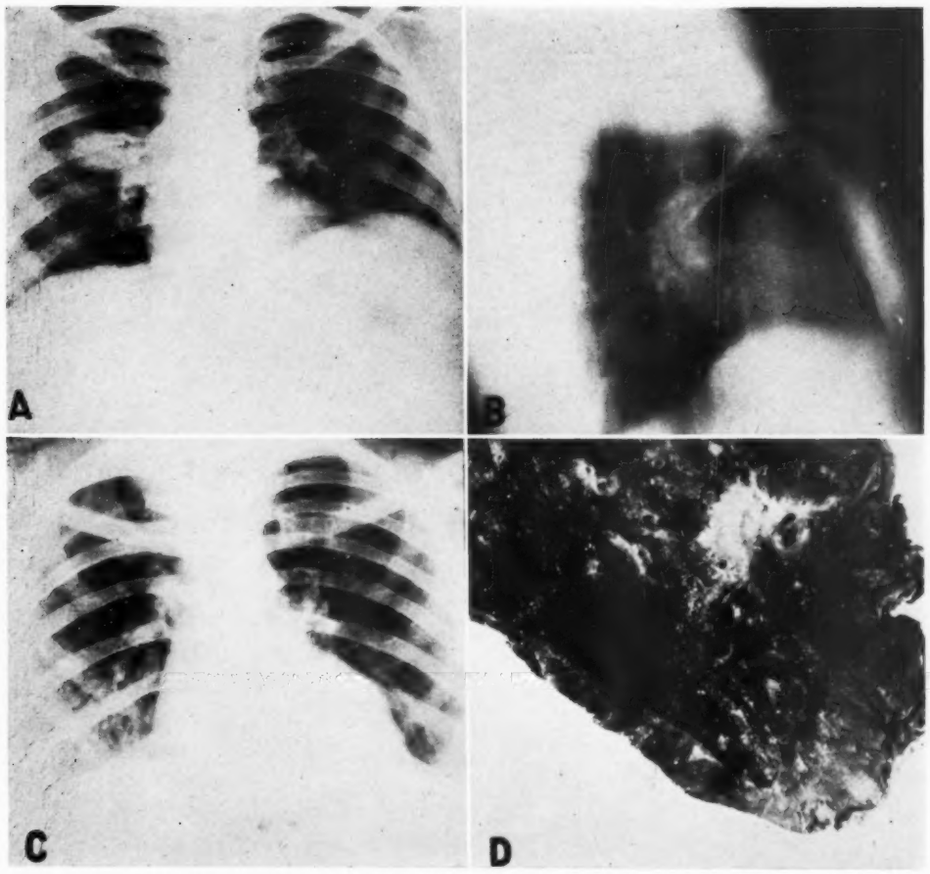


FIG. 5. Case v. L. K., an eleven year old Negro girl with an eleven-month history of tuberculosis. A, admission x-ray shows an area of density in the anterior segment of the right upper lobe. B, lateral tomogram after twenty-eight months' treatment shows an atelectatic anterior segment. Gastric cultures intermittently positive. C, x-ray of chest six months after operation. D, resected right upper lobe contains a dense central scar and a shrunken, bronchiectatic anterior segment.

Bronchostenosis: Destroyed Lung

CASE VI. M. M., an eight year old Puerto Rican girl, was admitted to Seton Hospital on January 9, 1951, with a history of cough and fever of one month's duration. Chest x-ray revealed complete opacification and contraction of the left lung with deviation of the trachea and heart to that side. (Fig. 6A.) One gastric culture contained acid-fast bacilli. Bronchoscopy revealed stenosis of the left main bronchus below the carina, the lumen being reduced to a transverse slit. Bronchography showed extensive bronchiectasis of the left lower lobe with absence of filling of the upper lobe bronchus. (Fig. 6B.) On August 23, 1951, left extrapleural pneumonectomy was performed. A markedly shrunken and fibrotic left lung was found. The postoperative course was uneventful. The patient is well and attending school. The specimen consisted of a completely destroyed lung replaced by dense scar tissue. (Fig. 6C.) The bronchus to the upper lobe was obliterated by fibrous tissue; dilated and distorted bronchi were present in the lower lobe. Microscopically, the only evidence of the initial tuberculous infection was the presence of an occasional tubercle with giant cells.

Comment. The destroyed lung, as encountered in this girl, resulted from bronchial obstruction by tuberculosis of the hilar nodes. The predilection of the left main bronchus to stenosis as a result of childhood tuberculosis is borne out by the preponderance of left pneumonectomies performed for this type of lesion.[2]

TUBERCULOSIS IN THE ADOLESCENT

Caseonecrotic Tuberculosis: Solitary Focus

CASE VII. M. W., a thirteen year old Negro girl, was admitted to Seton Hospital on June 30,

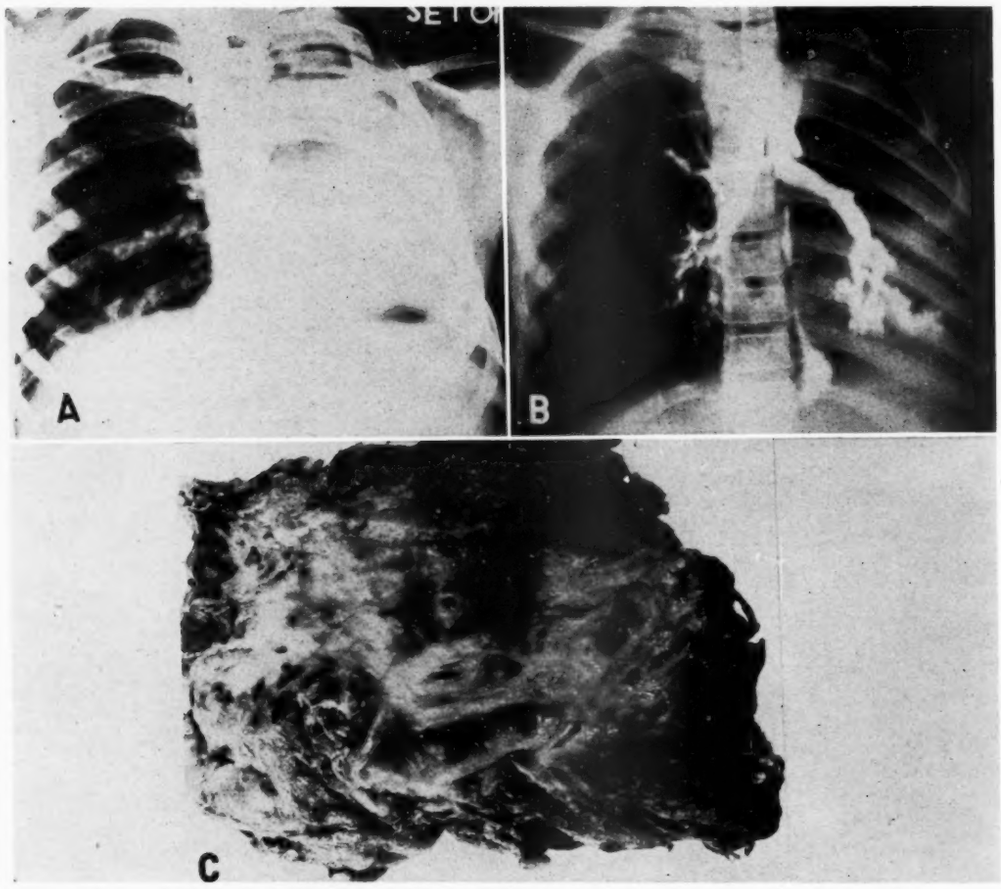


FIG. 6. CASE VI. M. M., an eight year old Puerto Rican girl with a destroyed left lung. One gastric culture positive for acid-fast bacilli. Bronchoscopy showed a transverse stenosis of the left main bronchus. A, admission x-ray disclosing a markedly shrunken left lung with mediastinal shift to that side. B, bronchogram reveals grape-like bronchiectasis of the left lower lobe and no filling of the left upper lobe bronchus. C, the left lung is completely destroyed and replaced by fibrous tissue.

1950, with a history of pulmonary tuberculosis discovered three months previously. Routine chest x-ray revealed an infiltration with central cavitation in the right upper lobe. (Fig. 7A.) Sputums were positive on direct smear for acid-fast bacilli. In October, 1950, right pneumothorax was induced, but soon abandoned because of extensive pleural adhesions. She was placed on streptomycin and PAS with little change in the radiographic appearance of the lesion. On March 6, 1951, right upper lobe lobectomy was performed. Postoperatively there was some delay in the re-expansion of the remaining middle and lower lobes. The patient's convalescence was otherwise satisfactory. The patient is well and attending school. The resected lobe was found to contain an irregularly shaped caseous mass about 3 cm. in diameter with a rim of lung tissue. (Fig. 7B.) Microscopically, the mass consisted of caseation surrounded by a zone of tuberculous granulation tissue and atelectatic lung. The bronchi and hilar nodes were uninvolved. There was little evidence of fibrous encapsulation around the lesion.

Comment. The central cavitation noted radiographically in this case was not confirmed by the pathologic findings. The lack of healing of the disease as seen by the absence of perifocal fibrosis after one year of treatment is to be noted. Such foci probably represent primary tuberculosis in the adolescent.

Caseonecrotic Tuberculosis: Confluent Nodular

CASE VIII. M. M., a thirteen year old Puerto Rican girl, had hemoptysis in February, 1950. She had been hospitalized elsewhere

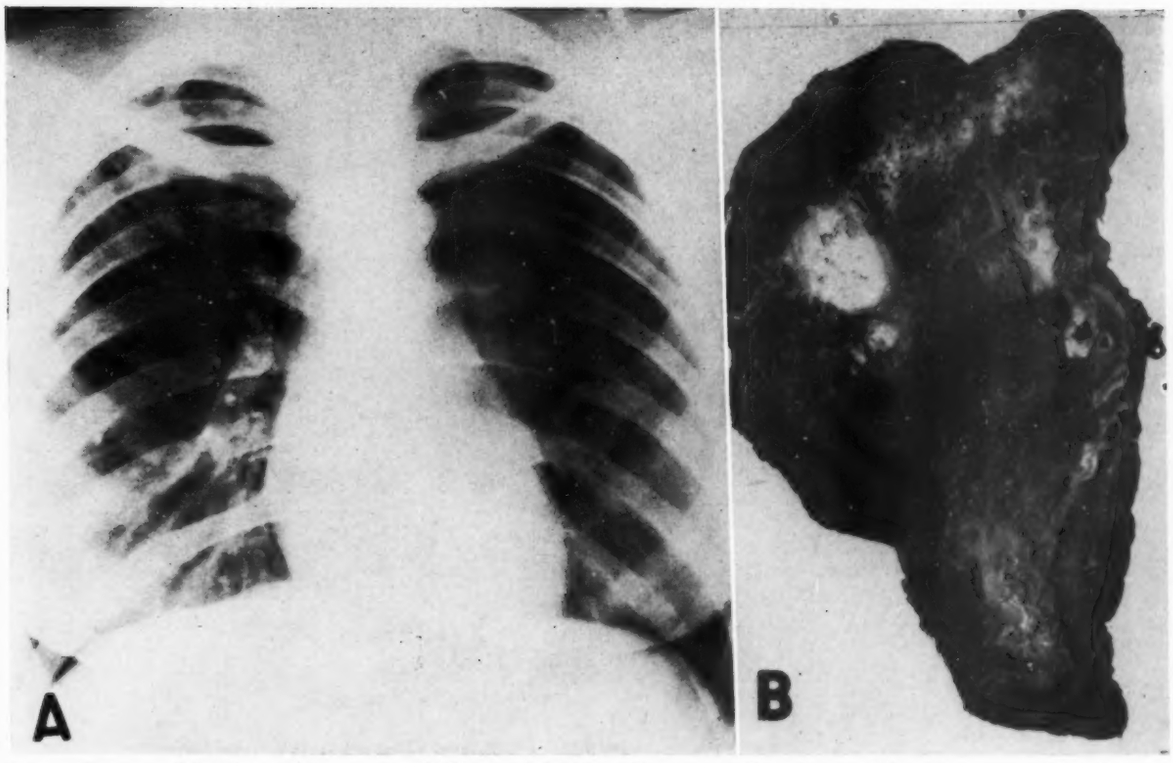


FIG. 7. Case VII. M. W., a thirteen year old Negro girl with pulmonary tuberculosis of the right upper lobe. Sputum positive for acid-fast bacilli. A, admission x-ray reveals an infiltration with cavitation in the right upper lobe. Patient was treated medically for one year. B, resected specimen shows a large caseous focus with little evidence of fibrosis.

where a cavity was found in the right upper lobe associated with positive sputum. (Fig. 8A.) At Seton Hospital she was placed on streptomycin and PAS with considerable diminution in the size of the lesion. On July 26, 1950, right upper and middle lobe resection was performed. Both lobes were found shrunken and diffusely nodular; the lower lobe free of disease. The patient had an uneventful recovery and has remained well since her discharge from the hospital. On gross examination there were noted numerous, caseous foci throughout both lobes which seemed to radiate outwards from the hilum. (Fig. 8B.) The microscopic findings revealed these nodules to be composed of confluent tubercles. Tubercles were also present in the hilar nodes. One large bronchus and a number of smaller ones showed endobronchial lesions.

Comment. This form of tuberculosis is frequently encountered in the adolescent. When first treated by resection we had considerable misgivings as to the value of extirpative surgery for this apparently disseminated type of disease. However, the patients have done well.

Caseocavitary Tuberculosis

CASE IX. A. W., a fourteen year old Negro girl, developed cough, chest pain and laryngitis in November, 1950. A diagnosis was made of pulmonary tuberculosis of the left upper lobe with cavitation. (Fig. 9A.) After admission to Seton Hospital on May 21, 1951, pneumothorax was attempted, but was unsuccessful. She was treated with streptomycin and PAS. The sputum was repeatedly positive for acid-fast bacilli. Bronchoscopy was negative. The patient improved clinically but the cavity in the left upper lobe persisted. On October 24, 1951, left upper lobe lobectomy was performed. Atelectasis of the left lower lobe developed in the immediate postoperative period which responded promptly to bronchoscopic aspiration. The patient was readmitted in April, 1952, to determine the source of an occasional positive gastric culture. Following cauterization of the bronchial stump the gastric cultures remained negative. The patient is well and attending school. On cut section the specimen showed a large cavity, 6 cm. in diameter, filled with caseous material. (Fig. 9B.) There were

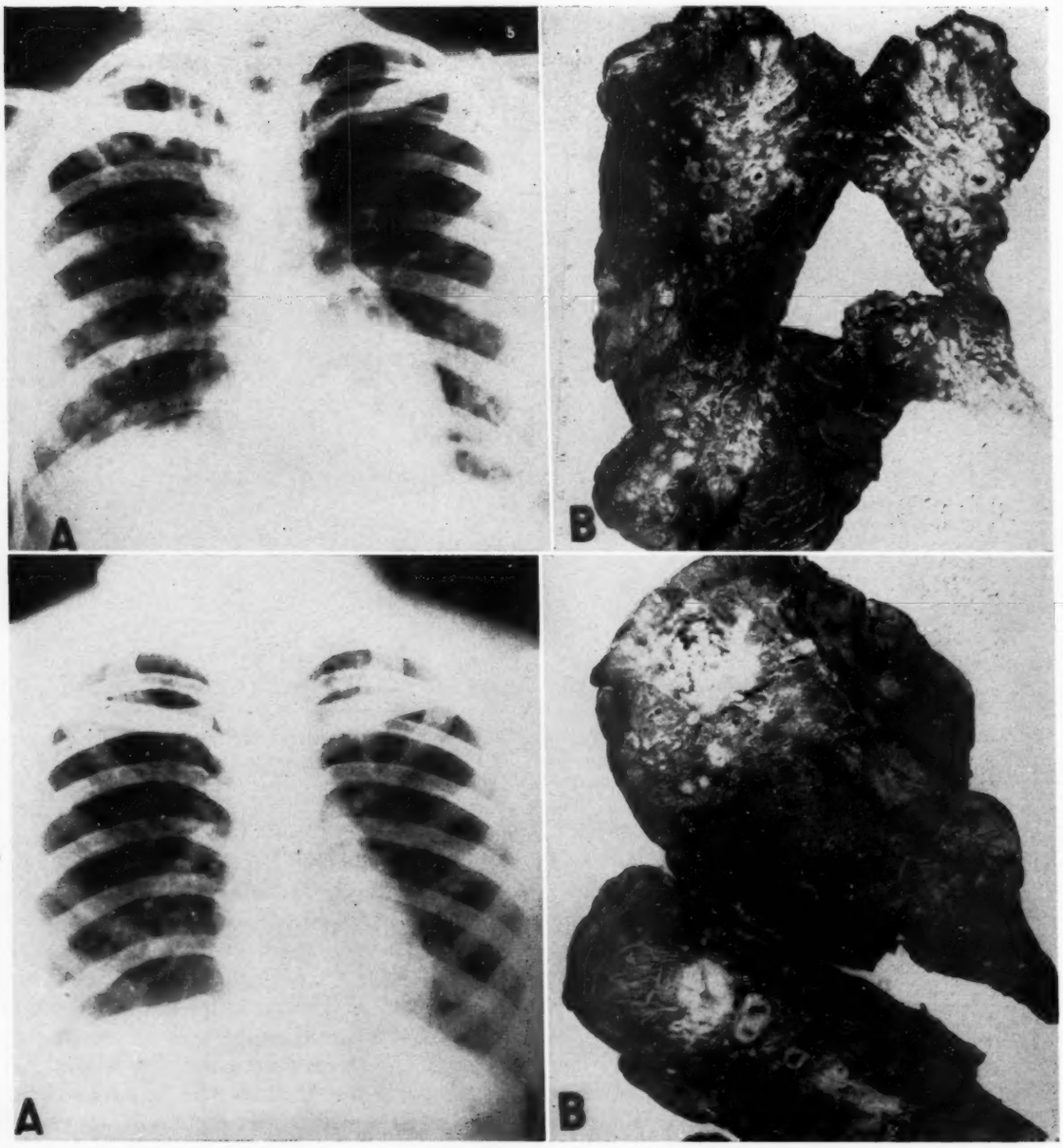


FIG. 8. Case VIII. M. M., a thirteen year old Puerto Rican girl with pulmonary tuberculosis of the right upper lobe discovered after an episode of hemoptysis. A, admission x-ray shows infiltration with cavitation in the upper lobe. Preoperative x-ray disclosed considerable clearing following a course of streptomycin. B, specimen shows caseous nodules throughout both lobes.

FIG. 9. Case IX. A. W., a fourteen year old Negro girl who had a cough and chest pain of six months' duration. A, admission x-ray showing infiltration with large irregular cavity in the left upper lobe. Sputum positive for acid-fast bacilli. The patient was treated for five months with streptomycin and PAS. B, resected left upper lobe shows an irregular cavity with surrounding caseous foci.

clusters of tubercles in the surrounding parenchyma. Microscopically, in addition to the cavity, there was extensive ulcerative tuberculous bronchitis.

Comment. The type of lesion encountered in this patient resembles closely that found in adults. The indications for excision were the presence of cavitation and positive sputum after a period of antimicrobial therapy. Involvement of the small bronchi is a common finding in the resected specimens in this age group.

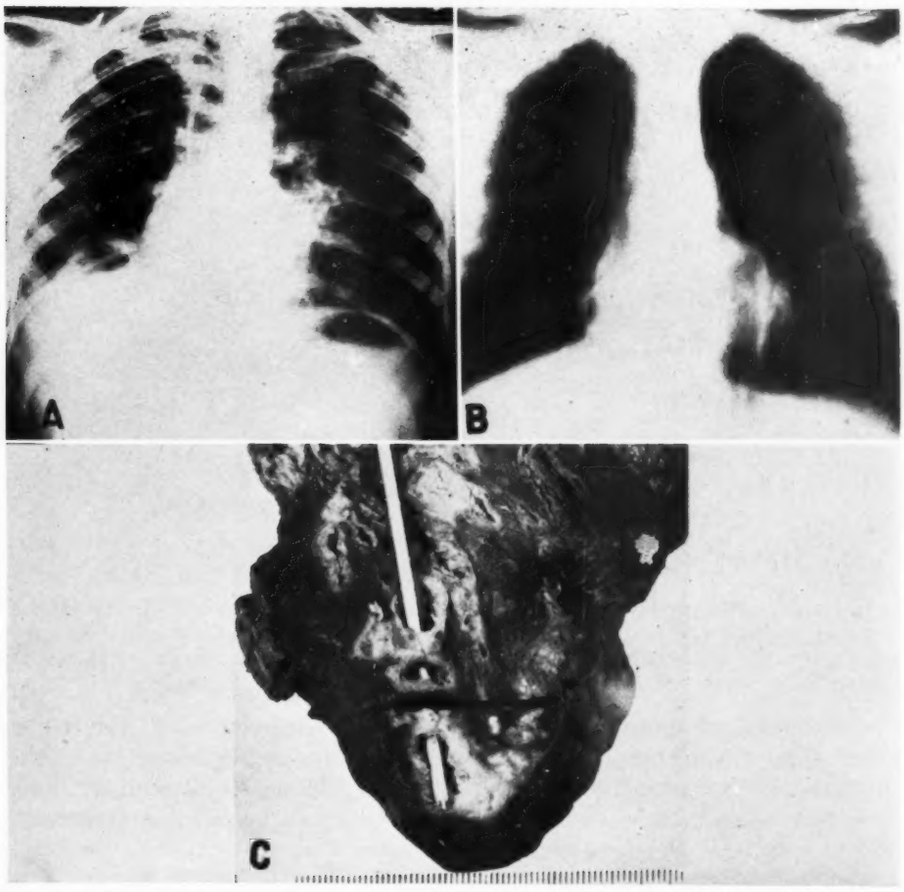


FIG. 10. Case XI. C. S., a thirteen year old Puerto Rican girl with bilateral pulmonary tuberculosis. A, admission x-ray shows bilateral disease with large cavity in the right lower lobe. B, after thirty-two months of medical treatment tomogram still shows a residual cavity in a shrunken and bronchiectatic right lower lobe. C, resected lobe contained extensive bronchiectasis and caseous tuberculosis.

Tuberculosis of Small Bronchi

CASE X. T. F., a 15 year old Puerto Rican girl, was found to have a minimal tuberculous lesion in a survey chest x-ray in April, 1950. She was given streptomycin by her physician for six months, which was continued for an additional four months at the Morrisania City Hospital. After her transfer to Seton Hospital on January 4, 1951, right pneumothorax was induced, but soon abandoned. Gastric cultures were repeatedly positive for tubercle bacilli. Bronchoscopy revealed edema of the orifice of the right upper lobe bronchus which subsided after a course of aerosol streptomycin and penicillin. Right upper lobe lobectomy was performed on May 7, 1951. The partly shrunken lobe contained many small nodules in the apical and posterior segments. The postoperative course was uneventful. Two months later bronchoscopy was performed to cauterize an ulceration of the bronchial stump. The patient is well and working full time as a bookkeeper. On cut section, indistinctly demarcated caseous foci were found throughout the specimen which seemed to radiate from the hilum. No cavitation was noted. Microscopically the lesions showed extensive endobronchial and peribronchial tuberculosis. In some areas the bronchial mucosa was ulcerated; in others, peribronchial tubercles were penetrating into the bronchial lumen.

Comment. The specimen in this patient showed predominantly bronchial tuberculosis with involvement of the entire lobe. The extent of disease noted in the specimen was in sharp contrast with the minimal radiographic findings.

Bronchiectasis: Destroyed Lobe

CASE XI. C. S., a thirteen year old Puerto Rican girl, was found to have bilateral pul-

FIG. 11. Case XII. H. W., a twelve year old Negro girl found to have tuberculosis on a survey x-ray. There were three admissions to the hospital during a three-year period for reactivations of the lesion. A, x-ray of the chest on last admission revealed a minimal lesion in the apex of the left upper lobe similar to the previous films. B, resected apicoposterior segment contains numerous caseous foci showing little evidence of healing.

monary tuberculosis with a large cavity in the right lower lobe. (Fig. 10A.) The patient was treated with pneumoperitoneum, streptomycin and PAS but her condition deteriorated. Improvement was noted for the first time in 1952 after the administration of isoniazid. During the following year her condition improved sufficiently to warrant consideration of resection of the shrunken right lower lobe which still showed a cavity. (Fig. 10B.) Preoperative bronchoscopy revealed narrowing and crowding of the bronchi in the right lower lobe. Functional studies showed adequate pulmonary reserve. On November 24, 1953 a right lower lobe resection was performed. At operation a markedly shrunken and indurated lobe was found adherent to adjacent structures requiring extrapleural mobilization. The postoperative course was uneventful. The patient was discharged and has remained well since her operation. The resected lobe was found to be shrunken and bronchiectatic. (Fig. 10C.) The dilated bronchi were filled with inspissated caseous material and had a grey shaggy lining. The atelectatic parenchyma contained confluent caseous foci. Microscopic examination revealed some of the bronchiectatic cavities to be lined with a thick hyaline membrane, others with tuberculous granulation tissue, some of which contained remnants of bronchial epithelium.

Comment. In this patient tuberculosis caused complete destruction of the right lower lobe. Prolonged antituberculosis treatment combined with resection achieved arrest of the disease.

"Minimal" Lesion

CASE XII. H. W., a thirteen year old Negro girl, was found to have a small lesion in the left upper lobe during an x-ray survey in March, 1949. She was admitted to Seton Hospital on May 5, 1949, and was discharged as an arrested case after ten months of bedrest. She was readmitted in March, 1951, for reactivation of the lesion and was given a course of PAS. Following discharge the sputum again became positive and the patient was admitted for a third time in March, 1952. (Fig. 11A.) The patient was placed on streptomycin and PAS. Bronchoscopy showed redness and swelling of the left upper lobe orifice which cleared with aerosol streptomycin. On July 31, 1951, resection of the apicoposterior segment of the left upper lobe was performed. The patient made an uneventful recovery. On cut section the specimen showed caseous foci from a pinhead up to 2.5 cm. occupying the entire thickness of the resected segment. (Fig. 11B.) Some were well defined; others poorly so. Microscopic examination showed the foci to consist of caseation surrounded for the most

part by a broad zone of very cellular and vascular granulation tissue studded with recent tubercles. Some of the foci had a thin fibrous capsule. Scattered tubercles were noted throughout the parenchyma.

Comment. This adolescent Negro girl demonstrates the instability of a minimal apical tuberculosis. Although the treatment during the first and second admissions may have been inadequate, according to present standards, it is doubtful if more intensive medical treatment alone would have healed the disease.

OBSERVATIONS

In dealing with pulmonary tuberculosis in childhood one is concerned with two types of disease: (1) primary infection in the very young and (2) postprimary disease in the adolescent. Not infrequently overlapping occurs, postprimary disease appearing in the child and primary in the adolescent. With the decline in tuberculosis late primary infection is occurring with increasing frequency. In the young primary tuberculosis tends to regress spontaneously and the management is medical. Surgery may be required in the treatment of sequelae of the initial infection. These are: (1) the large, stationary primary focus, (2) the primary cavity, (3) the persistently shrunken lobe, (4) symptomatic, postprimary bronchiectasis, and (5) the destroyed lung.

The primary focus may require resection if it is large and fails to regress or undergoes cavitation. Of the few such cases resected in this series, the caseous nature of the lesions was impressive. The significance of the primary focus as a potential site of later activation was shown by Nassau and Pagel.[3] In a study of thirty-two lobectomies and forty-five pneumonectomies, in patients with an average age of twenty-three years, they were able to differentiate three types of lesions: (1) large, round foci which were clear-cut instances of primary foci; (2) primary cavities, and (3) large, round foci in addition to calcified primary complexes found elsewhere. The first group consisted of twelve cases in which the majority were symptomless, discovered in routine or mass x-ray survey. Liquefaction was found in most of these foci; four showed early cavitation and caseous endobronchitis. Primary cavitation was found in eleven cases. Of the eight cases in the third category, inspissated cavities could be identified in two. The authors concluded that the lesions encountered, especially the cavities, must be regarded as potential or actual sources of phthisis. The large size of the lesions predisposed them to cavitation. The implication is clear that large primary foci which show no evidence of further regression are preferably treated by excision. This applies particularly to young Negro or Puerto Rican children with poor resistance to tuberculosis.

Pulmonary atelectasis due to primary tuberculosis is frequently encountered in children. The right middle lobe is particularly vulnerable to collapse. Graham and Hutchison[4] found the right middle lobe involved in thirteen of thirty cases of absorption-collapse in primary tuberculosis in childhood. As a rule re-aeration occurs when the infection in the hilar nodes regresses. Persistent atelectasis presents a problem in management. The children are usually in good health; the sputum or gastric washings do not contain tubercle bacilli. Aeration can occasionally be achieved by bronchoscopic aspiration or removal of caseous masses within the lumen. Many children, however, are found to have normal bronchoscopic findings since the obstruction is usually beyond endoscopic visualization. Persistent atelectasis of the lung may require resection. The five middle lobes resected in this series contained caseous tuberculosis, several of which probably represented the primary focus. It is doubtful if these lobes would ever have become restored to normal since they had been collapsed for long periods of time, the shortest for one year. The majority of so-called "middle lobe syndromes" encountered in adults have their origin in childhood.[5] Carlens and Hellström,[6] in a study of twenty-three cases of bronchial obstruction, found that in children with intrabronchial lesions only six of thirteen treated bronchoscopically showed re-expansion of the shrunken lobe in six months. In those with normal bronchoscopic findings where the obstruction was more distal, the collapse persisted, the affected lobes being the seat of fibrosis and bronchiectasis.

As might be expected from the frequency of atelectasis, bronchiectasis is also a frequent complication of primary tuberculosis in children.[7–11] In the majority the disease is symptomless and requires no special treatment. Surgery may be indicated if secondary infection supervenes, or if the bronchiectatic lung is the source of positive sputum or gastric cultures as

illustrated in Case IV. The importance of post-primary bronchiectasis as a source of positive sputum is brought out by Dijkstra[12] who, in 1952, reported six resections performed for this reason. Bronchography was necessary to delineate the disease in most of the patients. In a nine year old boy a totally destroyed left lung with extensive bronchiectasis was found, comparable to Case IV in the present series. In the remaining five, all teenagers, the tubercle bacilli disappeared from the gastric cultures and sputum after resection of the involved segments. The need for resection of a totally destroyed lung is obvious.

The indications for resection of pulmonary tuberculosis in the adolescent are comparable to those in adults and require little comment. The pathologic findings in the resected specimens have been very informative. The unstable and progressive nature of the disease is in keeping with the predominantly caseous nature of the disease. Particularly dangerous in this age group are the minimal apical lesions which may remain clinically dormant for a long period of time and then reactivate. Experience has shown that these foci tend to break down and excision is the treatment of choice after a suitable period of preparation with antituberculosis agents.

SUMMARY

An analysis of sixty-two children and adolescents with pulmonary tuberculosis treated by resection revealed the fact that the indications for surgery are influenced largely by the age of the patient. Children under the age of five rarely require surgery because one is usually dealing with a regressive primary disease. Resection may be required for irreversible changes in the parenchyma or sequelae due to bronchial obstruction.

In children six to ten years of age resection has a wider field of application. In this age group one is more apt to encounter sequelae of the primary infection, such as a shrunken lobe, bronchostenosis or bronchiectasis. Some children in this age group may have post-primary disease identical to that in the adolescent.

Resection is more often indicated for tuberculosis in the adolescent. The destructive nature of the disease which may not respond sufficiently to antituberculosis treatment calls for more radical measures.

REFERENCES

1. Rubin, M. and Mishkin, S. Resection for pulmonary tuberculosis in children and adolescents. *Surg., Gynec. & Obst.*, 95: 751, 1952.
2. Batelho, G. M., Chapchap, A., Pereira, H. L. G. and Cardeiro, O. V. Pneumonectomy in the treatment of tuberculosis in children. *Dis. of Chest*, 20: 642, 1951.
3. Nassau, E. and Pagel, W. The early changes of pulmonary tuberculosis in lobectomy specimens. *Tubercle*, 32: 120, 1951.
4. Graham, S. and Hutchison, J. H. Absorption collapse in primary tuberculous infection in childhood. *Arch. Dis. Childhood*, 22: 162, 1947.
5. Rubin, E. H. and Rubin, M. The shrunken right middle lobe. *Dis. of Chest*, 15: 127, 1950.
6. Carlens, E. and Hellström, B. Bronchial changes in children with primary tuberculosis of the lungs. *Acta paediat.*, 42: 43, 1953.
7. Hardy, J. B., Proctor, D. F. and Turner, J. A. Bronchial obstruction and bronchiectasis complicating primary tuberculous infection. *J. Pediat.*, 41: 740, 1952.
8. Williams, H. and Anderson, C. Bronchiectasis and bronchostenosis following primary tuberculosis in infancy and childhood. *Quart. J. Med.*, 22: 295, 1953.
9. Dickey, L. B. Primary pulmonary tuberculosis as a cause of bronchiectasis in children. *Dis. of Chest*, 21: 260, 1952.
10. Jones, E. M., Peck, W. M. and Willis, H. S. Bronchiectasis following primary tuberculosis. *Am. J. Dis. Child.*, 72: 296, 1946.
11. Hutchison, J. H. Post-tuberculous bronchiectasis in children. *Tubercle*, 32: 271, 1951.
12. Dijkstra, C. Persistent excretion of minimal quantities of tubercle bacilli in primary lung tuberculosis and its treatment by means of pulmonary resection. *Acta tuberc. Scandinav.*, 26: Fascicle 3, 1952.
13. Dijkstra, C. Resection-therapy for so called "minimal lesions." *Acta tuberc. Scandinav.*, 28: Fascicle 3–4, 1953.
14. Bentley, F. J., Grzybowski, S. and Benjamin, B. Tuberculosis in Childhood and Adolescence. London, 1954. Tavistock House North.
15. Ross, C. A. Pulmonary resection for tuberculosis in children. *Thorax*, 6: 375, 1951.
16. Levitan, M. and Zelman, M. Excisional surgical treatment of pulmonary tuberculosis in children. *Am. J. Dis. Child.*, 79: 30, 1950.
17. Auerbach, O. Tuberculosis in the adolescent. *Am. J. M. Sc.*, 201: 60, 1941.
18. Auerbach, O. Tuberculosis in children. *Am. J. Dis. Child.*, 75: 555, 1948.
19. Tsai, P. I. and Bashe, W. J., Jr. The complications and sequelae of primary pulmonary tuberculosis. *Quart. Bull., Sea View Hosp.*, 11: 129, 1950.

Surgical Treatment of Pulmonary Tuberculosis

NORMAN J. WILSON M.D., *Brookline, Massachusetts,* ORLANDO ARMADA M.D., WILLIAM B. O'BRIEN M.D. AND WILLIAM V. VINDZBERG M.D., *Wallum Lake, Rhode Island*

From the Rhode Island State Sanatorium and the Overholt Thoracic Clinic, Boston, Mass.

TODAY we are in the midst of a revolution in the treatment of pulmonary tuberculosis that began with the introduction of streptomycin for general use in 1947. The intervening years have witnessed the evolution of our present day concept of prolonged, uninterrupted drug therapy with the advent of para-aminosalicylic acid in 1949, isoniazid in 1951, and more recently pyrazinamide. These powerful antimicrobial drugs have proved to be capable of controlling a large percentage of the minimal and early moderately advanced lesions. In addition, they have proved to be remarkably effective in controlling toxicity, reducing excessive secretions, and bringing the patient into immunologic balance with his disease rather promptly. Even though cavitation or areas of caseation may persist, the drugs usually control the resolvable, pneumonic component of the disease process. The treatment of persisting cavities, areas of caseation and destroyed segments have become the lot of the thoracic surgeon in the drug era.

It is only natural that our concepts of surgical treatment have been changing continuously and rapidly during this period. All surgical procedures, especially resection, have been made safer by the better preparation of patients and the protection offered during surgery by the drugs. These facts plus improved anesthesia and increased experience on the part of the surgeons have caused resection to boom into its present place as the most commonly used surgical procedure in treating pulmonary tuberculosis. (Fig. 1.) Permanent collapse, especially of the type afforded by the extraperiosteal plombage technic, has maintained considerable favor in some clinics. Phrenic paralysis and pneumothorax have been literally abandoned. Antimicrobial therapy alone has supplanted these procedures in the treatment of early exudative or cavitary lesions. Experience has taught us that other procedures are more effective in permanently controlling those lesions which have already created irreversible pathologic changes in lung tissue.

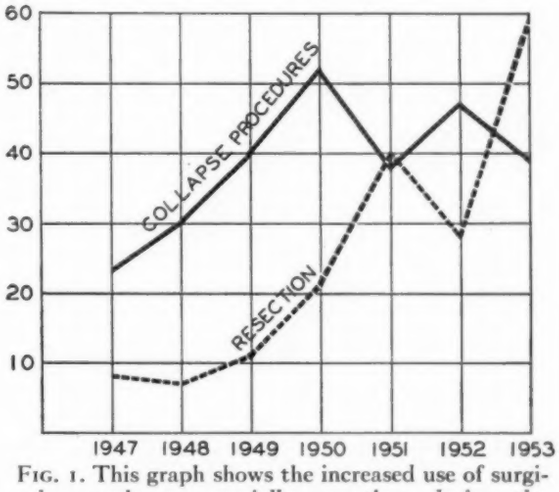


FIG. 1. This graph shows the increased use of surgical procedures, especially resection, during the drug era between 1947 and 1954.

In this era of rapidly changing concepts, it seems obvious that any dogmatic statement regarding the use of various procedures is out of order. As a result, the authors have elected to present our experience and the concepts used at the Rhode Island State Sanatorium during the drug era between January, 1947, and January, 1954. The discussion will be limited to the treatment of parenchymal lesions. Only the 411 unilateral surgical problems (not unilateral disease) will be considered. Eighty patients treated during this time with bilateral surgery have been excluded from this study because they are too complex for analysis, different procedures being used on the two sides in a high percentage.

The status of the 411 patients was evaluated

in July, 1954, providing a minimum of six months and a maximum of seven and one-half years of observation following operation; 260 were followed for at least two and one-half years and 335 for at least one and one-half years.

PREOPERATIVE EVALUATION OF SURGICAL PATIENTS

The patient's history is thoroughly reviewed. The duration of disease, the number of exacerbations, the social status of the patient, his ability to co-operate in long-term treatment and the history of previous drug therapy are vital points. Those with disease of long duration, chronic alcoholics, and those with previous or interrupted courses of drug therapy are less favorable candidates for any type of treatment, including surgery. A high percentage of the failures and complications reside in these groups. However, the paradox of the situation is that they are in need of surgical treatment more often than the more favorable groups and, therefore, constitute a significant portion of our surgical patients.

The roentgenograms from the beginning of the illness are reviewed. Only in this way can the major involvement, the degree of resolution and the proper evaluation of existing lesions be ascertained. A residual lesion involving a lobe or segment is frequently the only visible remnant of extensive disease that previously involved the major portion of one or both lungs. In such cases marked reduction of function must be suspected. In addition, the surgeon is apt to find at operation numerous nodules of varying size not seen on the x-ray. Postero-anterior, right and left anterior oblique views and postero-anterior laminagrams are routine. Lateral laminagrams are taken occasionally and probably will be used routinely when we gain more experience with them. These special x-ray studies are invaluable in localizing the disease and frequently demonstrate even cavitary lesions previously not seen by routine methods.

All prospective surgical candidates are fluoroscoped. Diaphragmatic and rib function are evaluated. This observation when combined with the patient's history, physical examination, serial x-rays and his ability to climb stairs gives a fairly accurate picture of his respiratory function. In addition, most patients have routine ventilatory studies including vital capacity, timed vital capacity and maximum breathing capacity. Those who have any evidence of limitation of function and almost all candidates for bilateral surgery are subjected to bronchospirometry to determine the function of each lung separately. The proper evaluation of respiratory function is considered to be of paramount importance. Otherwise, the surgery which may cure the tuberculosis may leave the patient a hopeless, miserable cripple.

Bronchoscopy has been performed routinely. Stenosis and residual ulceration are uncommon in these days of drug therapy. Residual redness of the mucosa is seen occasionally, but is not considered to be of importance even when resection is contemplated. If an ulcerating or granulating process is discovered, every attempt should be made to control the bronchial disease by a proper drug regimen prior to surgery.

CONTRAINDICATIONS TO SURGERY

The following conditions are the only absolute contraindications to surgery which we recognize regardless of the operation to be performed: (1) Inadequate cardiac reserve; (2) inadequate respiratory function to withstand the proposed procedure and (3) the existence of another disease process that is either uncontrollable or fatal.

Diabetes is not a contraindication to surgery. In fact, we believe that the prompt control of both the diabetes and tuberculosis is essential. These patients are treated more energetically than the non-diabetic patients. Surgery is used in a higher percentage.

In our opinion, surgery is not contraindicated by *pregnancy* prior to the last trimester. However, it is preferable to carry such patients to term on medical therapy if possible.

Persisting toxemia and *spreading infection* are rarely a problem now that we have more than one effective antimicrobial agent. However, occasionally such a patient is encountered. If possible, a change in the drug regimen may be effective. If medical treatment fails to control the disease and toxemia, we believe that surgery should be used provided the threatening lesion is unilateral. On numerous occasions, we have seen a carefully staged thoracoplasty or an adequate resection promptly change the

course of such patients. These patients do not necessarily have a low resistance to their disease. Not infrequently a careful pathologic study of a resection specimen will show bronchial strictures or large areas of caseation which have been mechanical factors militating against successful medical and drug therapy. Also, most of these patients have a low blood volume as a result of prolonged toxemia. Adequate transfusion will bring about a remarkable change in their clinical condition and enable them to undergo surgery without undue risk.

Age alone is not a contraindication to surgery. The youngest patient in this group was eight years and the oldest was sixty-six years of age. Many were over sixty years of age. Patients in the fifty's were common. As long as a patient's physical condition and physiologic reserves are adequate to withstand the required operation, we believe he should be operated upon. These elderly patients have tolerated surgery of all types remarkably well. We disagree strongly with those who deny these patients surgical therapy because of their age and state with a sense of false conservatism that they should keep their open cavities and exist as "good chronics." To die by inches inside an institution separated from friends and family is a severe and unjustifiable sentence to place on many of these elderly people.

COLLAPSE THERAPY

Indications. The indications for the various collapse procedures will be given under the appropriate headings. In general, however, the indication for collapse is residual cavitation that has failed to respond to medical treatment. The cavity should be located in such a position that it can be collapsed without involving a significant amount of normal lung. Residual cavity under 4 cm. in diameter in the apical-posterior segments of the upper lobes constitutes the ideal indication. Collapse therapy has no place today in the treatment of cavities in other positions, basal disease, solid lesions or those associated with bronchiectasis. Most cavities over 4 cm. in diameter and most destroyed lungs are treated preferentially by resection although, occasionally, coercing circumstances such as drug resistance or contralateral disease may cause the surgeon to elect thoracoplasty.

Staged Thoracoplasty. A conventional thoracoplasty is performed in stages, the superior ribs being resected first. The first rib and all transverse processes are removed. Prior to 1950, this was the most commonly used collapse procedure. In the early years of the drug era, patients were not prepared for or protected during thoracoplasty except in the substandard risks, streptomycin being reserved in case resection would be necessary at a later date.

Conventional thoracoplasty has the following disadvantages: (1) Multiple stages with the associated physical and mental strain for the patient; (2) multiple operations increase the cost of surgery and also limit the number of patients who can be treated in a given unit of time; (3) slow conversion of sputum; (4) paradoxical motion of the chest wall which interferes with both respiration and the cough mechanism. This predisposes to retention of bronchial secretions, spread of disease, and anoxemia; (5) deformity resulting from the scoliosis and abnormal position of shoulder girdle caused by resecting the first rib and transverse processes.

Because of these disadvantages, conventional thoracoplasty was abandoned by us in 1950. Since then, the standard thoracoplasty case with cavity under 4 cm. in diameter has been treated with plombage thoracoplasty to be described later. When larger cavities are treated by collapse, we employ a thoracoplasty performed from below-up. (Fig. 2.) The lower stage is performed first and, at the same time, an extrapleural mobilization of the cavity area is performed. The anterior portion of the lung is not mobilized. This wipes the cavity from the gutter area and from within the circle of the first rib and transplants it to a more lateral and anterior position. The cavity is placed thus into a more ideal position for collapse when the upper ribs are resected. In addition, the cavity frequently decreases in size between stages because of relaxation afforded by the mobilization. This type of mobilization differs from that performed with the first stage of a conventional thoracoplasty in that the narrowed thoracoplasty field below created by the first stage prevents the cavity from being dropped into a wide cushion of resilient lung tissue. The first rib is resected but all transverse processes are preserved. We have found it unnecessary to remove the processes if the gutter is completely developed and packed with oxycel. This has been the most effective collapse procedure for these advanced cases in our

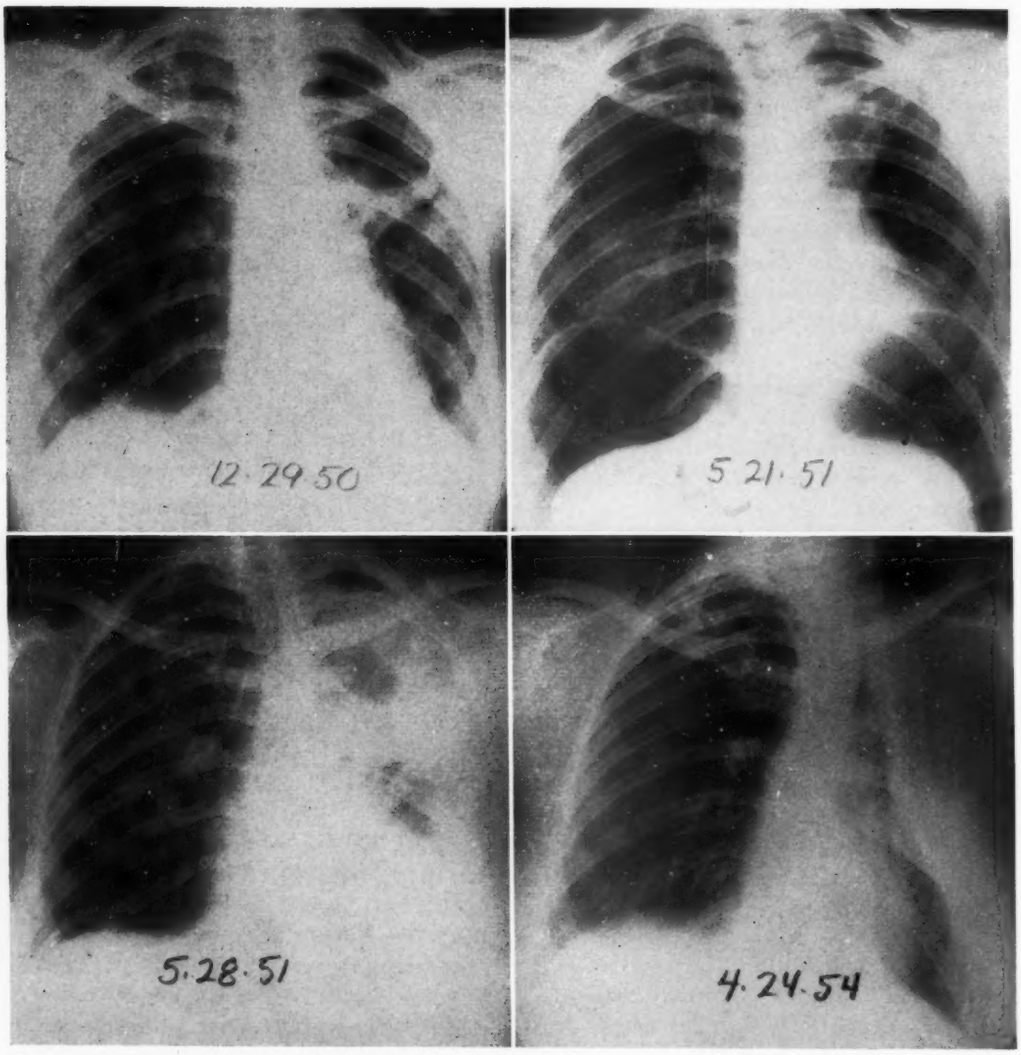
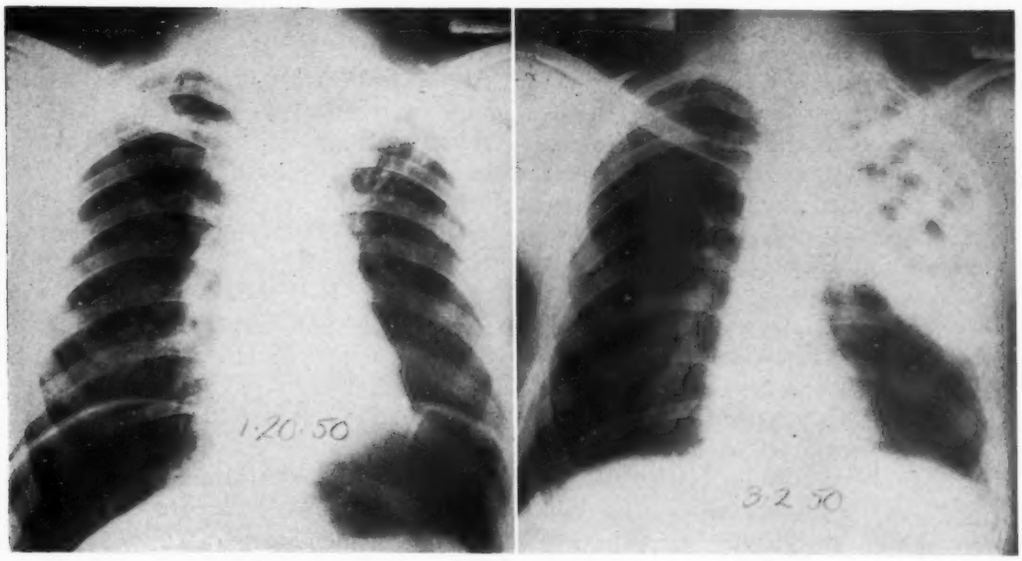


FIG. 2. A, roentgenogram of a twenty-four year old woman on December 29, 1950, on admission to the sanatorium. Note the giant cavity in the left upper lobe. Also the 3 cm. cavity in right upper lobe with scattered infiltration throughout upper half of lung. B, roentgenogram seventeen months later. Patient had been treated continuously with streptomycin, 1 gm. every three days, and P.A.S. daily. The cavity in right upper lobe is now closed. Giant cavitation persists in left upper lobe. The superior segment of the lower lobe was also involved. C, roentgenogram on May 28, 1951, five days following first (lower) stage of thoracoplasty with extrapleural mobilization. Note change in position of cavity. D, roentgenogram of April 24, 1954, approximately three years following surgery. Sputum has been negative consistently since operation. Patient has been asymptomatic and clinically well. She has gone through one pregnancy since operation.

hands. Its one disadvantage is that the extrapleural space is entered and may predispose to tuberculous wound infection. This has occurred in one case.

One hundred six patients were treated with staged thoracoplasty. In eighty-four (79 per cent) the disease was controlled by the thoracoplasty alone. Twenty-two had subsequent surgical procedures. At present fourteen patients (13 per cent) are dead and ninety-two (87 per cent) are living. Eighty-seven patients (94.5 per cent) of the living patient group are completely well.

The reader is again reminded that 94 of these 106 were operated upon prior to January, 1952, and 80 before January, 1950. None of these had the benefits of prolonged chemotherapy and many had no drug therapy at all. Case selection was also poorer at that time. Most of the complications and deaths occurred in these early cases. The fact that 95 per cent of the living patients are well speaks for a concept we



3A 3B

FIG. 3A and B. A, preoperative roentgenogram of a seventeen year old boy admitted to the sanatorium on July 10, 1948. Laminagrams revealed a cavity measuring 3½ by 2½ cm. B, roentgenogram after first stage of plombage thoracoplasty.

have held for many years, namely, that the patient who gets well with permanent collapse has a lasting cure that is hard to beat.

EXTRAPERIOSTEAL PLOMBAGE THORACOPLASTY

This operation (Fig. 3) was first performed at our institution in 1949. Since then, it has been found to be so safe and effective that it has become our favorite collapse procedure. The ideal indication is the persisting cavity under 4 cm. in diameter in the apical or posterior segments of the upper lobes. The collapse is created at one operation. The periosteum is stripped only from the undersurface of the first rib. The number of ribs and the length of ribs stripped of periosteum below the first rib depends upon the extent and distribution of the lesion as determined by oblique roentgenograms and laminagrams. The collapse is designed to compress the diseased areas and to avoid collapsing normal segments of the lung. As many as eight ribs have been stripped at one operation. In spite of this, one of the outstanding features of this operation is the lack of shock. The ribs are left intact and the extraperiosteal space is snugly packed with 1¼ inch lucite spheres inside a polyethylene wrapping. (This prevents the spheres from migrating between the ribs and makes their removal at any later time a simple procedure.)

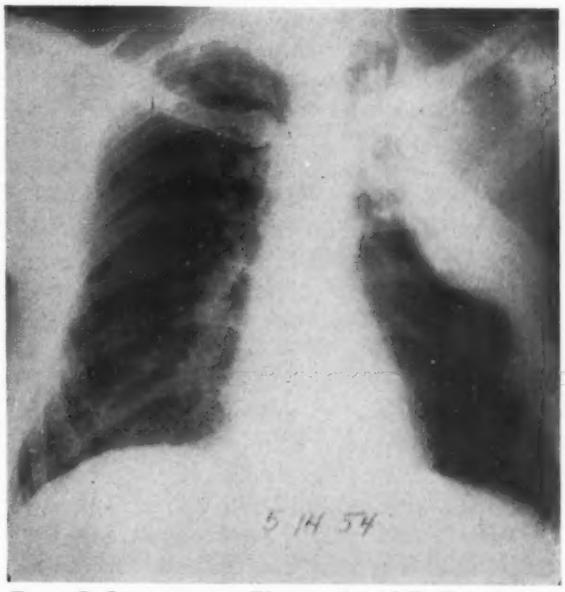


FIG. 3C. Same case as Figure 3A and B. Roentgenogram of May 14, 1954, four years after operation. The patient is clinically well and working.

One week following operation the antimicrobial drugs are stopped unless there is an active endobronchial lesion or a contralateral lesion that indicate their use. Only in this way can the collapse failures be determined early. If drugs are continued, the sputum may remain negative even though the disease is uncontrolled. We like to have collapse therapy work

on its own merits and likewise believe it is important to pick up our failures early. After four months of careful sputum studies, a decision as to further surgery is made. If the sputum is negative, a second stage is performed removing the plombage and resecting the previously deperiostealized sections of ribs. The first rib and all transverse processes are left intact to avoid significant deformity. If the sputum remains positive, a resection is performed and the second stage of the thoracoplasty completed at the same time. Thus regardless of the success or failure of the plombage, the patient's treatment consists of a maximum of two operations.

One of the problems to be settled is the safety of leaving the plombage in place and avoiding the second stage. Our experience to date would indicate that the plombage material is well tolerated for periods up to two or three years. However, more time will be required to settle this question. For this reason, a two-stage operation is performed on the younger, good risk patients. In those over fifty-five years of age, in the bilateral cases and in those with marginal functional reserves we have performed one-stage procedures leaving the plombage permanently in place. There has been only one infection of the extraperiosteal space. This occurred in the first few months after operation and was caused, we believe, by a technical error during the first stage when the extrapleural space was entered and widely exposed.

The advantages of plombage thoracoplasty are many: The collapse is created at one operation. Conversion of sputum occurs rapidly. Paradoxical motion of significance is eliminated. As a result, there is less interference with respiration and cough. Retained secretions and spreads are truly rare. Fewer stages reduce the strain on the patient and the cost of surgical treatment. The first rib and all transverse processes are preserved so that no significant clinical deformity occurs even though the roentgenogram shows a slight scoliosis. Functional studies have shown that the functional loss is small and is more predictable than with either staged thoracoplasty or resection. One of the greatest advantages is that the failures can be treated with resection with a total of two operations. The treatment of collapse failures is certainly an easier task and is more successful than is the case with resection failures. Another factor of great importance is that this procedure, as is true with any thoracoplasty, can be used with much more safety than resection in those patients who harbor bacilli resistant to the antimicrobial drugs. Last but not least of the advantages is that experience has taught us that this is the simplest and safest of all major surgical procedures used in treating tuberculosis.

One hundred forty patients have been treated with unilateral extraperiosteal plombage thoracoplasty. In 120 (86 per cent) is was successful. The twenty failures have undergone resection. No deaths have occurred from any of the operative procedures and no deaths caused by tuberculous infection have occurred. Three have died, two of coronary occlusions and one of metastatic carcinoma. One hundred thirty-seven (97.8 per cent) are living and of these, 127 (92.7 per cent) are completely well. Three patients are known to be alive and active but we were unable to get accurate follow-up data for evaluation.

The results with this procedure have been so good that we have been reluctant to shift as completely to resection as have most clinics.

Extrapleural Procedures. Four extrapleural pneumothoraces have been performed. This procedure was used chiefly in young patients who had not attained full growth. Thoracoplasty is not used in these young patients because of the marked scoliosis and deformity that results. These were done prior to 1951. Today such patients would be treated either by resection or extraperiosteal plombage, delaying the second stage until after full growth had been attained.

Nineteen extrapleural plombage thoracoplasties have been performed. The indication here has been the poor risk patient with marginal respiratory function. This procedure has the advantage of leaving the thoracic cage intact and is reversible at any time during the postoperative period since the plombage can be removed without creating paradoxical motion of the chest wall. As our experience with the extraperiosteal plombage has increased, the extrapleural approach has been used less and less. We have not had the disastrous experience with this procedure recorded in the literature. This is attributed to the following factors: (1) protection of drugs, (2) careful selection of patients, (3) leaving the mediastinal pleura intact and (4) removing

the plombage at the end of four to six months and performing a thoracoplasty of a type that preserves the first rib and the transverse processes.

These procedures have been limited to the treatment of small cavities above the level of the second anterior rib. This explains the good results. All twenty-three of the patients are alive and well. In one case the follow-up data are inadequate. The remaining twenty-two are well and have a persistently negative sputum.

Summary of Results with Collapse Therapy. The following statistics include the morbidity and mortality of the original collapse procedures plus those of all other procedures used subsequently in the treatment of the patients.

1. Two hundred sixty-nine were treated initially by collapse therapy between 1947 and 1954. Sixty-four per cent were operated upon before the era of long term chemotherapy (1952).

2. Eleven (4.0 per cent) tuberculous complications occurred during the postoperative period of sixty days.

3. Thirty (11 per cent) tuberculous complications occurred late.

4. There were two (0.7 per cent) postoperative deaths. These occurred in those treated by staged thoracoplasty prior to 1950. Since 1950, 176 collapse therapy patients have been treated with no postoperative deaths.

5. Fifteen (5.5 per cent) have died following the 60 day post-operative period.

6. Two hundred fifty-two (93 per cent) of the patients are living and, of these, 236 are clinically well with negative sputum. This represents 88.5 per cent of the total group or 94 per cent of the 252 living patients.

7. The study of the 163 treated by collapse procedures other than staged thoracoplasty is quite significant. There were no postoperative deaths. Only three late deaths have occurred, caused by coronary occlusion in two and metastatic carcinoma in one. One hundred sixty (98 per cent) patients are living and of these, 149 (93 per cent) are completely well. Of the remaining eleven, four are known to be alive but we have inadequate follow-up data on them; four are clinically well but have either a positive sputum or unstable roentgenogram; and three have either active or progressive disease.

CAVERNOSTOMY

Cavernostomy is used rarely. In two instances of giant cavitation it was combined with thoracoplasty. The cavernostomy was performed prior to the thoracoplasty to reduce the size of the cavity and thus limit to some extent the amount of collapse required.

In only one case has cavernostomy been used alone. This patient previously had bilateral pneumothorax and was left with a large cavity in the superior segment of the right lower lobe. Her respiratory reserve contraindicated resection. Cavernostomy followed several months later by a muscle flap plastic closure of the residual cavity was effective in controlling her disease.

Cavernostomy is used occasionally as a palliative procedure in hopeless cases with large cavities causing excessive cough and expectoration. Dramatic symptomatic relief frequently is accomplished.

Open cavernostomy is used at our clinic. This is performed in one stage if the pleura is adherent and in two stages if it is free.

RESECTION

In the chemotherapeutic era, resection has increased in popularity until it is now the most commonly used of all surgical procedures in treating pulmonary tuberculosis. This has been the result of improved anesthesia, increased experience with resection, and the effect of the antimicrobial agents which bring the patient to surgery in better condition and protects him during the postoperative period. Many clinics now boast that they rarely use any other surgical procedure. In our opinion, this can be said only if operation is withheld from many patients who should be treated surgically. Any team of physician and surgeon who is willing to extend their surgical program to include the aged and those with marginal function must be willing and capable of using not only resection but every type of collapse procedure and occasionally even cavernostomy.

Although all types of resection are being employed more frequently, the use of segmental resection has increased phenomenally. It is an especially appealing operation to physician, surgeon and patient in that it permits extirpation of the offending lesion with the preservation of almost a maximum of normal lung tissue. The acceptance of seg-

mental resection as a rational approach in the treatment of tuberculosis was delayed by the concept that tuberculosis is a disseminated disease. Even though this is true, exploration of early tuberculous lesions has demonstrated that the major necrotic lesion is often confined to one or two segments. In addition, the drugs frequently cause such complete resolution of the disease process that the residual, necrotic lesion is well contained in a segment or even a subsegment of the lung. These facts plus the surgeons increased experience with the procedures have led to its acceptance.

Indications. The following are considered to be absolute indications for resection: (1) Associated suppuration, (2) tuberculous bronchiectasis, (3) thoracoplasty failure, (4) bronchial stenosis, (5) uncontrolled lower lobe disease, (6) tuberculoma-like lesions whether they represent true tuberculomas or inspissated cavities and (7) cavity in an inexpandible lung with or without associated empyema following pneumothorax.

Resection is considered to be the operation of choice in the following types of cavities: (1) Giant cavities, (2) cavities which have manifested evidence of recurring tension and poor drainage, (3) cavities in poor position for collapse such as those which hug the mediastinum and (4) cavities in the anterior segment of upper lobes or lying below the fifth rib posteriorly so that a large volume of normal lung would be sacrificed in collapsing them.

Where widely disseminated, predominantly unilateral disease has created a destroyed lung, we prefer to use resection although thoracoplasty can be used with success in many of these cases. We believe that resection is more effective and reduces the number of operations. Gaensler and Strieder[1] have shown that thoracoplasty over destroyed lungs causes significant reduction of maximum breathing capacity whereas resection adds little, if any, functional impairment.

Resection may be indicated to control hemorrhage that has been refractory to all other methods of treatment. This is a rare indication. We have never encountered it. When it does arise, it represents the most serious of situations and should be performed only as a life-saving procedure.

One of the biggest problems that has arisen as a result of drug therapy is the question concerning which residual lesions should be resected. A negative sputum is no longer a reliable guide because of the suppressive action of the drugs. The examination of resected specimens has proved that our present x-ray technics, including laminagraphy, are not entirely reliable. Cavities are found at times in the specimen when not suspected preoperatively. However, it is more common to find no cavity when one has been indicated by the roentgenographic study. Our policy has been to resect any residual necrotic focus 2 cm. or over in size and totally destroyed segments or lobes. As time goes by and more experience with long-term chemotherapy evolves, we may find that resection of many such lesions is unnecessary to cure the patients and prevent recurrences. On the other hand, we may learn that these residual foci are a source of recurrence and that drug therapy has merely delayed the day of exacerbation. The problem of whether the tubercle bacilli are dead or alive in the residual focus has never been of concern to us. We are aware that many of these organisms will not grow on culture or produce disease in the guinea pig. However, until much more bacteriologic and clinical evidence is available, we have decided to consider the bacilli to be virulent and capable of causing exacerbation of disease.

The smaller residual areas of caseation have been treated medically. Wedge excision of such foci have not been part of our surgical program. A high percentage of patients remained well with this type of disease even before the drug era.

Primary versus Secondary Drug Treated Cases. The ideal case for resection is the patient with unilateral, localized disease under treatment with primary, uninterrupted drug therapy. Our experience has led us to the conclusion that resection can be used in such cases with safety at anytime provided the following criteria exist: (1) Adequate respiratory reserve; (2) resection is the primary surgical approach to the problem; (3) the lesion is confined within the unit of lung to be resected whether this be segment, lobe or an entire lung and (4) resection is applied as soon as ideal conditions have been secured with bed rest and antimicrobial drugs. This means that toxemia and excessive bronchial secretions have been eliminated and that active lesions in other areas of the lung have been controlled.

Once these criteria have been met, resection can be performed with safety regardless of the operative procedure used. The presence of open cavity and/or positive sputum have not altered statistics. Likewise, those resected with only a few weeks of preoperative drug therapy have withstood operation just as well as those who have had six months or more of preparation. Once resection has been decided upon, there is little justification to sacrifice the patient's time to permit inspissation of a cavity or further contraction of irreversibly damaged lung.

Our experience has been different with those patients who have had previous courses of drug therapy. The morbidity and mortality are higher in this group of patients. In addition, longer periods of preoperative preparation seem to reduce the number of complications. If possible, such patients should be treated with those drugs found to be effective by sensitivity studies on the sputum. Many other factors in addition to previous drug therapy contribute to the increased trouble incurred in treating these patients. They have disease of longer duration; a higher percentage have had previous collapse or surgical treatment; and their average respiratory reserve is lower. Several patients in this group resistant to streptomycin and isoniazid have been treated with pyrazinamide. This drug has been very effective in protecting them from tuberculous complications.

The type of tuberculosis, the functional reserves of the patient, and the availability of effective chemotherapy are factors which determine good or bad results much more than the type of resection used.

Results. Table 1 summarizes the results with resection. The morbidity and mortality rates for pneumonectomy and lobectomy plus segmental resection are higher because the worst cases fall into these groups.

TABLE 1

RESECTION FOR UNILATERAL SURGICAL PROBLEMS—1947 TO 1954

	Pneumonectomy	Lobectomy	Lobectomy plus segmental	Segmental	Wedge
Number of cases	68	70	9	24	3
Postoperative tuberculous complications	8	2	1	2	0
Late tuberculous complications	13	6	1	0	0
Postoperative deaths	2	1	1	1	0
Late deaths	5	0	2	1	0
Living patients	61 (90%)	69 (98.6%)	6 (67%)	22 (92%)	3 (100%)
Per cent of living patients well with negative sputum	93	93	100	96	100

Thirteen (7.5 per cent) of the 174 resections had tuberculous complications in the postoperative period: fistula with empyema five; contralateral spread or exacerbation three; sinuses in wound two; ipsolateral exacerbation one; contralateral pleural effusion one and extrapulmonary tuberculosis one.

Twenty (11.5 per cent) late tuberculous complications occurred: fistula with empyema one; empyema two; contralateral exacerbation eight; stump ulcer seven and ipsolateral exacerbation two.

There were five (2.9 per cent) postoperative deaths caused by: fistula and spread one; pulmonary edema one; pulmonary insufficiency one; pulmonary embolus one and blood dyscracia one.

The eight (4.6 per cent) late deaths were caused by: coronary occlusion one; cor pulmonale three; fatal hemorrhage from an empyema space one; progressive tuberculosis two and leukemoid metaplasia one. This last

complication was considered to be due to tuberculosis of the bone marrow although never proved.

One hundred sixty-one (92.5 per cent) of the 174 patients are alive and 151 (94 per cent) of these are clinically well. Fifty per cent of the patients were operated upon prior to January, 1952, and did not have the benefit of long-term chemotherapy.

POSTSURGICAL CARE OF PATIENTS

During the first three months following surgery, patients are kept on modified bed rest. Bathroom privileges and permission to eat in a dining room in the convalescent ward is permitted. The patient's activity is slowly increased during the next seven to nine months. During this time, the sputum is carefully studied and periodic roentgenograms are taken. The patient is then considered for discharge from the sanatorium. The majority of patients are then ready to return to part-time work and most of them return to their previous occupations.

Prolonged chemotherapy is given following all resections since it is assumed that tuberculous tissue was transected and new lesions were created even though they may not be manifest. Prolonged chemotherapy is also prescribed for collapse therapy patients who have had bilateral surgery or have had active lesions in other areas of the lung other than the collapsed area. Drug therapy is stopped one week following the optimal collapse procedures so that the failures can be discovered.

SUMMARY

The introduction of antimicrobial drugs has created radical changes in the surgical treatment of pulmonary tuberculosis. Resection is now used more frequently than any other procedure. However, our statistics indicate that the prognosis depends more on the control of the open lesion than upon the type of surgery used. This is demonstrated by the fact that between 93 and 96 per cent of the living patients treated by the various surgical procedures are clinically well. In our experience the lesion adequately controlled by collapse has an equally good prognosis as those resected. The key to successful surgical treatment of tuberculosis is the selection of the simplest and safest procedure which will permanently control the disease.

REFERENCE

1. Gaensler, E. H. and Strieder, J. W. Progressive changes in pulmonary function after pneumonectomy. *J. Thoracic Surg.*, 22: 1–34, 1951.

Segmental Resection for Pulmonary Tuberculosis

J. Maxwell Chamberlain, M.D., *New York, New York*

In the surgical management of pulmonary tuberculosis segmental resection is now an established and accepted procedure.[1–28] It can be used in all stages of pulmonary tuberculosis provided the major offending focus is limited to one or two segments of the lobe. The percentage of sputum conversion is high and with experience the morbidity and mortality rates are low. The operative technic is moderately intricate and demands a great deal of postoperative vigilance. When the operation is performed early, it avoids prolonged hospitalization and, by corollary, reduces the task of rehabilitation. Its greatest virtue, of course, is its preservation of pulmonary function as was intended by its originator, Dr. E. D. Churchill[29] and other early workers.[30–33]

BASIC PATHOLOGY

Pulmonary tuberculosis usually begins as a "patch" of indolent pneumonia confined to the upper and posterior segments of the lobes as reported by Medlar and others.[34–36] Less frequently it may involve a lobe or the entire lung but regardless of its dimensions it begins as pneumonia. The pneumonia may take three courses: (1) resolution, (2) fibrosis or (3) caseation necrosis. If resolution of the exudative element occurs, the alveolar walls remain intact, no function is lost and ultimately all evidence of the disease disappears from the chest film. If fibrosis occurs, the area is replaced by "scar" tissue (the productive reaction), alveolar function is lost and the x-ray film always reveals the site of the insult. In other instances small "patches" of pneumonia coalesce to form a large conglomerate area. If the vascular nutrition to the center of this area is lost, caseation necrosis occurs and the alveolar architecture is destroyed. Usually one or more small bronchi communicate with the necrotic area; and should liquefaction of this caseous material occur, the area "shells out" to form a cavity.

Probably all three factors are at work in every lesion. There is some resolution, some fibrosis and some caseation necrosis. It is the necrotic focus, and especially the size of this focus, that threatens the patient's future welfare. Through liquefaction of this necrotic area bronchial dissemination of the disease may occur. Segmental or subsegmental resection performed at the proper time is designed to avoid such spreads.

BASIC PHYSIOPATHOLOGY

The functional advantages of leaving behind only one of three segments of a lobe was at first debatable. It was reasoned, however, that as a functional unit it contributed its bit to the total function and as a "filler" it prevented excessive distention of the residual lung components and in this way preserved their function. We now know by actual bronchospirometric measurement performed on a series of these patients before and after segmental resection that little or no function is lost and in some cases it seems to be actually improved.

Adhesions may determine which segments will enlarge to compensate for the healing and contraction in the diseased segments. For example (Fig. 1), adhesions between the right posterior segment and the chest wall (A) will not permit enlargement and upward movement of the lower lobe as healing and contraction occur in the apical and posterior segments (B). However, with the hilum of the lung as an axis, a counterclockwise enlargement of the anterior segment and the middle lobe is often observed. On the other hand if adhesions exist between the right apical segment and the thoracic vault (Fig. 1C) as healing and contraction occur, the lower lobe enlarges and rises high in the pleural cavity. (Fig. 1D.) In such cases there is less demand for the anterior segment and middle lobe to enlarge. Segmental enlargement is greatest in cases free of adhesions. Conversely, an obliterative pleuritis

seems to prevent not only the contraction of the diseased segments but also any significant enlargement of the healthy components.

INDICATIONS

The main indication for segmental resection is the necrotic lesion. Necrotic lesions may be to exudative, fibrotic or necrotic disease. It may be reasoned, though not without an element of doubt, that if the lesion has been present in serial x-rays for some time, it is predominantly a fibrocaseous lesion. In other words, the acute exudative or pneumonic elements have probably resolved. If, however, the

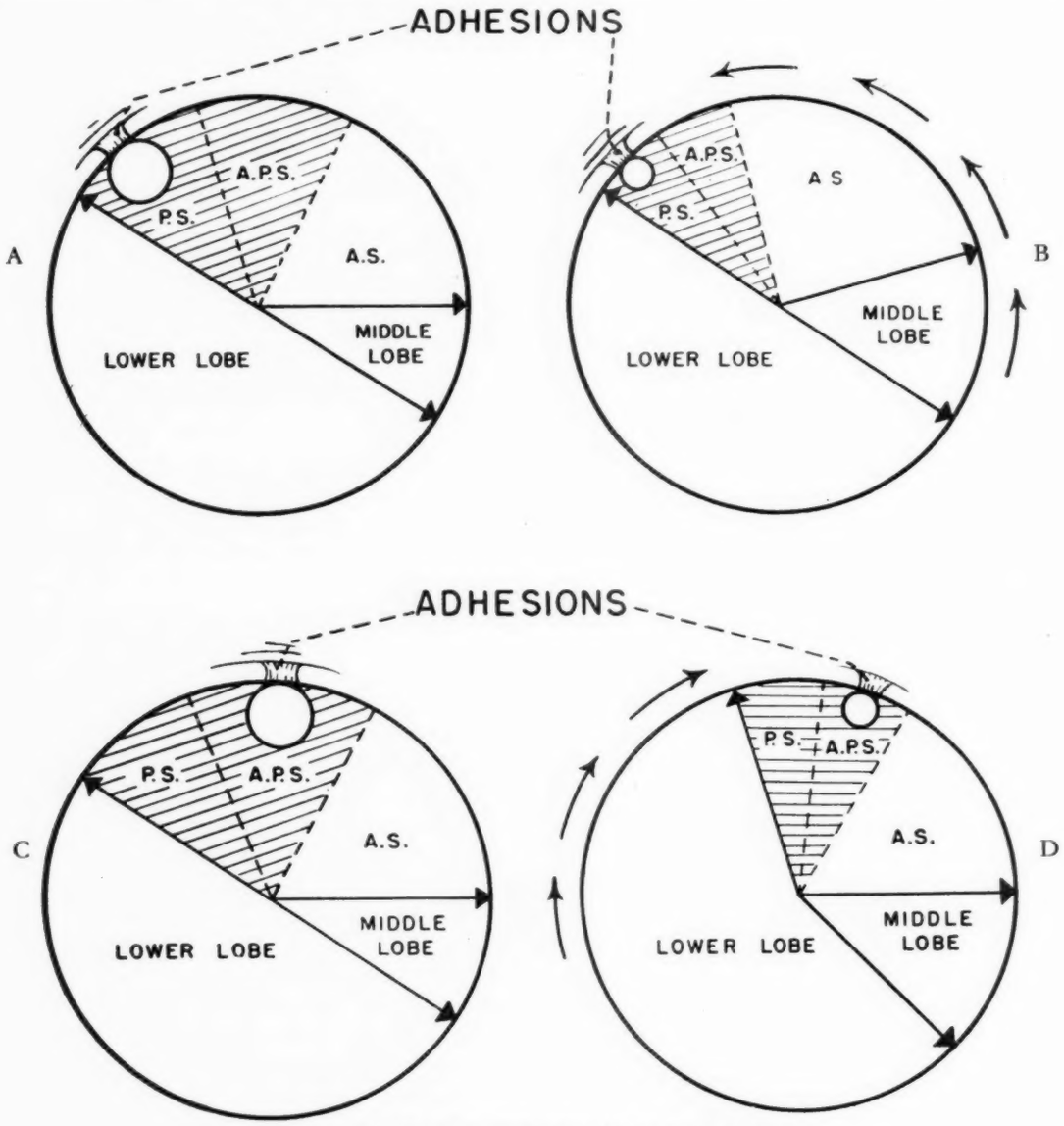


FIG. 1. A to D, segmental clock (right lateral view).

small, medium or large and still confined to one or two segments of a lobe. Not only is the size of the necrotic focus important but also its duration, and especially the amount of associated exudative or pneumonic disease.

The duration of the lesion is significant because it is difficult in the chest film to distinguish the boundaries between shadows due shadow is being viewed for the first time this assumption may be inaccurate.

The size of the necrotic focus is important because the small foci are drained in most instances by small bronchi and the large ones are drained by large bronchi. It seems reasonable to suppose that the caseous material undergoing liquefaction will drain more easily

through a large bronchus than through a small one, and perhaps it follows that it "spreads" more easily as well. These points require further proof.

Exudative disease can be expected to respond to conservative management and antibiotic therapy permitting the dimensions of the surgical procedure to be reduced. Emergency operations have been successfully performed in the presence of acute tuberculous pneumonia, in the presence of hemorrhage, cavity rupture and extensive pneumonic "spreads" but, in general, major thoracic procedures, including thoracoplasty, should not be done in the presence of significant exudative or pneumonic disease.

The ideal indication for segmental resection is the fibrocaseous lesion with or without a cavity and devoid of an exudative element. The focus should be of such size and duration that mature medical opinion is doubtful of the patient's future security.

PREOPERATIVE STUDY AND PREPARATION[17]

Lateral section laminagraphy stressed by Klopstock[3] gives an extremely valuable preview to the thoracotomy. The phrase "bloodless thoracotomy" applied to laminagraphy seems justifiable to those accustomed to its use. Perhaps no other preoperative study is more helpful to the surgeon.[2,38,39] The exact location of the disease, and especially the appearance of the segments to be left behind, may be learned from these lateral laminagraphic sections. As experience in the use of laminagraphy increases, it is rare for the surgeon to perform a lobectomy when a segmental resection was intended. If a segmental resection is contemplated, resection is unnecessary, the chest being entered through an intercostal incision since a tailoring surgical procedure after a segmental resection is usually avoided.

The specific antibiotics are given for variable lengths of time prior to the operation, but always until the exudative element surrounding the fibrocaseous focus is thought to be absent. Other preoperative studies are similar to those which should precede any major surgical operation.

TECHNIC OF OPERATION

The segments to be removed have been decided upon prior to operation as a result of lateral laminagraphy, and the bronchi to these segments are immediately isolated and clamped before unnecessary manipulation or mobilization of the lung. (There are anatomic exceptions to this plan.) After the segmental bronchi have been clamped and divided, the lobe is then mobilized with impunity since secretions can no longer be expressed into the bronchial tree. Occasionally, after palpation our interpretation of the laminagraphs proves inaccurate and it is necessary to remove an additional segment or subsegment.

Isolation, ligation and division of the arteries are next accomplished. Preservation of the intersegmental veins is desirable when only one segment is removed, but when two segments are removed it is necessary to remove the intersegmental vein with the specimen. The intersegmental plane is then developed by gentle traction and dissection as described by Clagett.[32] Bleeding from the raw area is meticulously controlled. No effort is made to cover the raw area with pleura as was previously described;[6] any attempt to approximate the raw edges will only distort the segment and interfere with its ability to "breathe." Furthermore, were the raw area to be closed, in all probability the sutures would cut out in the next few days during deep breathing or coughing. The bronchus is then reamputated and closed with interrupted silk sutures. Pleuralization of the bronchial stump is not always done. Usually the residual segment or adjacent lobe seals the bronchus upon complete re-expansion. Two tubes are left in for drainage and re-expansion. One tube is anterolateral and fixed with a suture to the pleura of the thoracic vault. The other tube is low and in a posterolateral position. The wound is closed in anatomic layers and a small *narrow* dressing is applied in order to facilitate auscultatory examination of the chest during the immediate postoperative period. The large *tight* dressing physiologically simulates the so-called captive lung mechanism. Unilateral tidal loss is significant.[40] The two tubes are connected to a "Y" tube and placed upon active suction.

POSTOPERATIVE REGIMEN

The residual segments are inflated at the completion of the hilar dissection and the intrapleural suction is established simultaneously with wound closure. Approximately 200 cc. of saline solution are left in the pleural cavity to dilute the small amount of blood which gravi-

tates to the dependent parts of the hemithorax during wound closure. The dilution of blood by the saline solution prevents clot formation and helps to insure patency of the tubes during the early postoperative period. Most of the saline solution is immediately removed by the suction system as wound closure is completed. A compact portable suction pump is used to maintain the desired intrapleural pressure during transportation from the operating room. This maneuver, though not essential, is an additional precaution to insure immediate and complete re-expansion of the residual lung components.

At first the patient's position in bed is on the side of the operation. Later he is turned to his back and for effective coughing he is allowed to assume the sitting position. Young people with muscular diaphragms will tolerate slight elevation of the foot of the bed. This allows the fluid to gravitate to the thoracic vault and keeps the costophrenic angle sharp. The fluid is then removed through the upper tube and the pleural reaction is confined mainly to the thoracic vault. "Pleurisy" which binds or fixes the diaphragm may significantly influence function. Pleural reaction in the thoracic vault is of little functional significance.

Intrapleural suction is usually set at a minus 15 to 25 cm. of water. Pressures at a minus 5 to 10 cm. of water are physiologic. End-operative studies on the bronchospirometric contribution of the individual lung have revealed that pleural suction in the range minus 5 to minus 16 in fact results in a control subtidal, ipsilateral ventilation. Maximum tidal volume occurs with negative pressures in the range of minus 18 to minus 20. It should be noted that Lindskog found experimentally that reinflation via collateral ventilation requires a gradient of some 16 cm. of water.

The bronchi and bronchioles must not become occluded by blood or secretions if the segments are to remain inflated. Clots of blood in the small bronchioles may be propagated to larger and larger bronchial divisions to produce a segmental atelectasis. On the other hand, if a good reverse air flow is maintained up through the bronchioles and out through the small alveolar leaks, secretions do not collect to account for subsegmental or segmental atelectasis. In our experience active suction does not prolong alveolar leaking. In the majority of cases the tubes can be removed in forty-eight to seventy-two hours. Tubes are never removed at night. It seems preferable to remove them in the morning when a full complement of nurses and doctors is available, should a pneumothorax develop. A roentgenogram is taken a few hours after the tubes have been removed with a portable chest x-ray machine to determine the degree of lung expansion. A sterile trocar, cannula and catheter are always available and suction is re-established immediately should a "late leak" develop. Complete and early re-expansion seems essential in the prevention of an empyema or bronchopleural fistula.

Patent airways, large and small, are essential to successful re-expansion. Ciliary action, bronchial peristalsis (elongation and fore-shortening of bronchus during the respiratory cycle) and cough are the patient's protection against spreads and atelectasis. The patient is urged by the nurse to take thirty deep breaths every half hour during his waking hours. Furthermore, he is encouraged to help turn himself in bed frequently. This exercise promotes deep breathing. However, intratracheal suction each morning and night during the first forty-eight hours is perhaps the most important postoperative assistance the patient can be given. Its disagreeable aspects, if nothing else, assures patient cooperation throughout the day whenever he is urged to cough by the nurse in attendance.

Pain is caused by the incision, muscle spasm, the divided ribs and the pleura. Little can be done about the incisional pain. The muscle spasm can be reduced by frequent passive and active shoulder girdle exercises. Fixation of the divided ribs during closure will prevent pain arising from the fracture site, but pain from the pleura is more difficult to control. The parietal pleura is very sensitive and the visceral surface of the residual segments is altered; (1) by operative manipulation (gauze abdominal pads, sponges, etc.); and (2) by the precipitation of fibrin as a result of the mild but ever present hemothorax. The movements of these residual lung components against the parietal pleura, plus the pleural irritation of the drainage tubes, are probably responsible for most of the pain. This theory is supported further by the fact that patients after a pneumonectomy have much less pain than patients after a lobectomy or a segmental resection.

The control of pain is extremely important

since coughing and deep breathing are painful. Narcotics, not sedatives, will control pain. Their frequent use is encouraged in moderate doses. The use of narcotics in chest disease earned its bad reputation in the primordial stages of our learning. Modern vigilant nursing and a regimented postoperative plan will not allow the patient to slip into narcotic coma and drown in his own secretions.

Specific antibiotics are used routinely after operation. They are continued for various lengths of time as determined by the attending physician, usually for not less than three months. The non-specific antibiotics are used one day before surgery, at operation and for the first week after surgery. Non-tuberculous empyema and wound infections have played no significant role in our experience. Transfusions are used during and after operations to maintain blood volume. Usually 1,500 to 2,000 cc. of blood is given each patient.

Ambulation is permitted during the first two weeks after operation to encourage costal and diaphragmatic breathing. Early restricted activity may lead to high fixation of the diaphragm and cause a corresponding decrease in respiratory function. The patient returns to bed after two weeks and remains there usually for three months except for lavatory privileges. Activity is then increased again.

The use of oxygen in segmental resection is important in the older patient, but it is rarely necessary in the young patient with good coronary circulation. The temporary costal and diaphragmatic restriction after operation creates a "shunt" and the oxygen saturation of the blood does not return to normal for a variable number of days. In the older patients the coronary circulation is an unknown factor. In this group the generous and prolonged use of nasal oxygen is encouraged. Nasal oxygen seems preferable since these patients require a great deal of nursing attention which is difficult to administer if an oxygen tent is used.

Abdominal distention with elevation of the diaphragm is a frequent postoperative complication which may embarrass respiration. Clear fluids are given the first day supplemented by intravenous fluids if necessary. On the second day nourishing liquids, soups, custards, etc., are usually tolerated. However, an unexplained elevation in pulse rate in a patient who is not vomiting may be an indication for gastric decompression. In muscular young men gastric distention is not as obvious as in atonic women or older men. Acute gastric distention, therefore, should be suspected in every muscular young man whose fluid intake is adequate, but who remains thirsty, runs a rapid unexplained pulse and is *not* vomiting.

An upright x-ray film is taken on the first postoperative day with a portable machine. A second is taken on the day the tubes are removed (usually the second or third postoperative day). A third is taken on the fourth or fifth postoperative day. After that the patient is well enough to stand for fluoroscopy at frequent and regular intervals. Such vigilance is necessary since "late leaks" seem to occur in about 5 to 10 per cent of the patients, and immediate intercostal intubation will avoid the complications associated with the unexpanded lung. On several occasions we have had to intubate a patient more than twice. A late leak developed in one patient on the fourteenth postoperative day, one day before discharge. In another patient it did not develop until the forty-first postoperative day. The "late leak" is considered a minor complication because these patients need not return to the operating room for intubation and it is extremely rare for the "late leak" to progress and cause a major complication, such as empyema or bronchial fistula.

COMMENTS

Pulmonary tuberculosis is usually bilateral though not necessarily bilaterally active. The advocates of segmental resection must admit that only the major offending focus or foci are removed by this procedure. The foci are almost always present in the opposite lung or in the residual lung components on the side of the operation, but it should be remembered that these foci are also present in patients successfully treated by other forms of therapy such as bed rest, pneumothorax or thoracoplasty. Removal of *all* of them is technically impossible and probably unnecessary. The decision to remove other foci is dependent upon size and location.

The actual size of the hazardous lesion is difficult to estimate in centimeters. Usually a large lesion is more hazardous than a small one, but on the other hand a small lesion in a patient without resistance can be more hazardous than a much larger one in a patient who seems "unable to handle his disease." Furthermore, it is

noted by those in the field of experimental research, by the pathologist and by the clinician, that lesions in the anterior and dependent segments of a lobe are less hazardous than those in the posterior and apical segments. Cavities located anteriorly are recalled only because they are exceptions to the rule or because they began in the apical-posterior segments and extended into the anterior and dependent areas. A lesion requiring resection in the superior segment[6] of the lower lobe may safely remain in the tip of the lingula. To molest the various lobes by attempting to remove locally all foci, large and small, without regard for location ignores this basic information and subjects the patient to unnecessary morbidity and perhaps mortality. This belief is based not only upon our recent and short experience with the segmental resection, but upon a comparatively long experience with the thoracoplasty procedure: for instance, though the therapy has changed, the location of tuberculosis is the same. Therefore, there must have been foci anteriorly in the days when the thoracoplasty was our most popular form of surgical therapy. Yet our thoracoplasty failures were not usually due to the "breakdown" of lesions anteriorly where the collapse was least, but due to unclosed cavities posteriorly where the collapse was greatest. It is not implied, however, that tuberculosis located anteriorly should not be respected.

Overdistention of the residual segments after segmental resection is less than after lobectomy and pneumonectomy. Physiologically, respiratory function is inversely proportional to the degree of emphysema caused by overdistention. Lung elasticity is variable,[40] and in all patients with tuberculosis there exists a variable amount of emphysema. Laennec, without a microscope, described focal emphysema surrounding every healed and contracted lesion. The physiologic effects of overdistention are much more noticeable in the older patient with horizontal ribs and a thick anteroposterior diameter than in the slender young patient with oblique ribs and a comparatively narrow chest. There must be a limit to the amount of distention a lung can tolerate before actual alveolar wall destruction occurs. The speed and duration of overdistention are also factors. Tuberculosis is an indolent disease which heals slowly. As healing and contraction of the diseased segments occur, a slow compensatory enlargement of the healthy parenchyma takes place. The undesirable aspects of *suddenly* demanding a single lobe to fill one chest after a lobectomy has led us to believe that a small tailoring procedure should be done simultaneously.

Overdistention may or may not be responsible for the "breakdown" or reactivation of disease in the residual segments. A point less debatable is the fact that should a breakdown occur the emphysematous patient does poorly with tuberculosis and usually to an extent inversely proportional to the amount of emphysema. It is thought that one of the factors responsible for such a response in the emphysematous patient is the interference with the cleansing mechanism. The patient's protection against "spreads" is enhanced by an effective cleansing mechanism: (1) ciliary action, (2) bronchial peristalsis and (3) cough. Bronchial peristalsis consists not only of changes in the diameter of the bronchial lumen but changes as well in the length of the bronchus during inspiration and expiration. In the overdistended lobe the bronchus is not only distorted by its new position but is relatively fixed and permanently elongated. The amount of foreshortening is reduced. Furthermore, the amount of residual or "stagnant" air is increased and the amount of tidal or "movable" air is reduced and an effective cough is dependent upon *movable* air. Therefore, not only is overdistention undesirable from a physiologic viewpoint but from a pathologic one as well.

Obliteration of the dead space simultaneous with the segmental resection is done to avoid complications. When an obliterative pleuritis is present, the adhesions may prevent the compensatory enlargement of the healthy components and a rather large space remains after the resection of two or more segments. This space may be obliterated in two ways: (1) by a small tailoring thoracoplasty (costectomy) and (2) by extraperiosteal plombage without rib removal.

The small tailoring costectomy removes short segments of second, third and fourth ribs posteriorly. The first rib may or may not be included. If not, the periosteum on its lower surface is mobilized with the others. The risk of the additional surgery and the paradoxical chest seems justifiable.

The extraperiosteal plombage reduces scoliosis and the amount of paradox. The procedure

is the same as described except that the periosteum on the outer surface of the ribs is preserved, the ribs are not removed, and the extraperiosteal "plomb" may consist of (1) the patient's own subscapular collection of blood, (2) many sheets of gelfoam® or (3) a plastic sponge encased in a polyethylene bag.

TABLE I
NINE DEATHS

Primary Operation—3 (1%)		
W. M.	2nd postoperative day	?Coronary occlusion
G. A.	4th postoperative day	Contralateral pneumonia
W. F.	12th postoperative day	Lower nephron nephrosis
Secondary Operation for Bronchopleural Fistula—4(1.3%)		
Other—2 (0.7%)		
A. M.	9 mo. postoperatively of bronchopleural fistula	
G. S.	2 yrs. postoperatively of alcoholism	

In obliterative pleuritis mobilization of the lower and middle lobes is not done when the preoperative fluoroscopy reveals good movement of the diaphragm. Should the lobes be mobilized, the diaphragm usually rises to follow their ascent into the thoracic vault. The division of the many adhesions provokes oozing and "sweating" of blood which may result in a hemothorax to bind and restrict diaphragmatic movement. The functional loss from a small tailoring surgical procedure in the thoracic vault is less than that due to the risk of diaphragmatic fixation.

RESULTS

A series of 300 consecutive patients who had segmental resection for pulmonary tuberculosis has been followed for one to five years. At the present time 93.7 per cent are living and well, 3.3 per cent living with disease and 3 per cent are dead. (Table I.)

The type of operative procedure was as follows: 210 (70 per cent) had segmental resection only; 32 (10.7 per cent) had lobectomy plus segmental resection; 31 (7 per cent) had bilobar segmental resection; 35 (11.7 per cent) had local excisions only; 2 (0.7 per cent) had right upper and middle lobectomies combined with resection of the superior segment of the right lower lobe. The significant major complications were bronchopleural fistula, tuberculous empyema and spread. (Table II.) In addition one patient had hemorrhage from a small pulmonary vessel and required reopening of the wound for ligation. Another patient required decortication twenty-four days after operation to obtain complete re-expansion of the lung.

There were nine deaths. (Table III.) Three patients died as a result of the operation. Patient W. M., who was apparently progressing satisfactorily, died suddenly on the second postoperative day presumably from coronary artery disease. Autopsy did not definitely disclose cause of death. Patient G. A. did very well for two days after operation. X-ray review at that time showed clear lung fields, but late in the afternoon of the second day the patient began to show signs of contralateral pneumonia. Death occurred two days later. Postmortem examination revealed the contralateral lung to be heavy, gelatinous and essentially free of purulent secretions. Four patients died as a result of secondary operations to correct bronchopleural fistula and tuberculous empyema. M. P. had hemorrhage from a subclavian artery which was involved in the tuberculous empyema. Control was impossible and he died two days later. D. G. died of an anesthetic accident after pneumonectomy had been completed for bronchopleural fistula. L. G. died nine days after thoracoplasty and partial resection of the right lower lobe to correct bronchopleural fistula. The fistula was controlled but

TABLE II
THREE HUNDRED SEGMENTAL RESECTIONS FOLLOWED ONE TO FIVE YEARS

	No.	Per cent
Living and well	281	93.7
Living with disease	10	3.3
Dead	9	3.0

TABLE III
MAJOR COMPLICATIONS

	No.	Dead	Persistent	Controlled
Bronchopleural fistula	16(5.3%)	5(1.7%)		11(3.7%)
Empyema	13(4.3%)	5(2.7%)	1(0.3%)	7(2.3%)
Spread	9(3%)	5(1.7%)	1(0.3%)	3(1%)

the limited functioning lung tissue was not sufficient to support the patient. F. W. died after multiple procedures to correct fistula which persisted. A. M. died nine months after operation with a persistent bronchopleural fistula. An acute bronchitis was the contributing factor to the final episode. G. S. had a segmental resection for tuberculosis and was well with negative culture and clear x-ray films, but he was found dead in bed apparently due to alcoholism two years after operation.

TABLE IV
EXACERBATIONS

Resolved	
Antibiotics only	5 (1.7%)
Additional surgery	6 (2%)
Persistent	7 (2.3%)
Total	18 (6%)

There have been eighteen exacerbations in the entire series. (Table IV.) Eleven have resolved with further surgery or antibiotic therapy; seven persist. About two-thirds of these occurred immediately or within the first six months and the remainder at scattered later intervals after operation. The late exacerbations have not represented a serious problem in these patients.

Eight patients had planned bilateral resection and two required unplanned contralateral resection for pre-existing disease.

SUMMARY

1. The basic pathology of tuberculosis is an indolent pneumonia which may (1) resolve, (2) fibrose or (3) caseate. Usually all three elements are present in every lesion.

2. The basic physiology is not significantly changed by segmental resection, because only the diseased components are removed and compensatory mechanisms have already been effected.

3. The indication for segmental or subsegmental resection is a fibrocaseous lesion with or without cavitation confined to one or two segments of a lobe, but still large enough that mature clinical opinion is doubtful of the patient's future security.

4. The preoperative preparation is the same as for any major operation with special attention to laminagraphy and especially lateral laminagraphy.

5. An anatomic segmental resection is done for moderate and far advanced lesions. In minimal lesions a wedge resection or local enucleation is possible. Subsegmental resections may also be done anatomically.

6. Postoperative care must be vigilant. Patent airways (intratracheal suction), the control of pain, the use of antibiotics, the obliteration of dead space by complete reexpansion of the lung using active suction and checked by frequent postoperative x-ray examinations are important to a successful result.

7. Tuberculosis is usually bilateral though not bilaterally active. Only the major active focus is removed by segmental resection. The importance of other foci is dependent upon the size and location. Anterior foci are less hazardous than those posteriorly.

8. The problem of overdistention is not great after segmental resection, but obliteration of the dead space is essential to success. Occasionally, a periosteal plombage procedure without resection of the ribs is done in deference to this principle.

9. In obliterative pleuritis mobilization of the lung is not done when the preoperative fluoroscopy reveals good diaphragmatic movement. The functional loss is less if a small tailoring surgical procedure is done in the thoracic vault.

REFERENCES

1. GILBERT, L. Pulmonary resection; report of early results. *Quart. Bull. Sea View Hosp.*, 9: 222–233, 1947.
2. CHAMBERLAIN, J. M. and KLOPSTOCK, R. Segmental resection in pulmonary tuberculosis. Preliminary report. *Tr. Nat. Tuberc. A.*, 45: 181, 1950.
3. KLOPSTOCK, R. Discussion of Paper by Scannel, J. G. An anatomic approach to segmental resection. *J. Thoracic Surg.*, 18: 72, 1949.
4. CHAMBERLAIN, J. M. and RYAN, C. H. Segmental resection in pulmonary diseases. *J. Thoracic Surg.*, 18: 199, 1950.
5. SAMSON, P. C. Discussion of Paper by Chamberlain, J. M. and Ryan, C. H. Segmental resection in pulmonary diseases. *J. Thoracic Surg.*, 19: 220, 1950.
6. CHAMBERLAIN, J. M. and KLOPSTOCK, R. Further experiences with segmental resection in pulmonary tuberculosis. *J. Thoracic Surg.*, 20: 845–853, 1950.
7. PLIEGO, J. and CHAMBERLAIN, J. M. Pre- and postoperative treatment in pulmonary segmental resection. *Rev. mex. de tuberc.*, pp. 36–47, Nov.–Dec., 1950.
8. CHAMBERLAIN, J. M. Pulmonary segmental resection in tuberculosis. *Rev. mex. de tuberc.*, pp. 48–54, Nov.–Dec., 1950.

9. Chamberlain, J. M., Storey, C. F., Klopstock, R. and Daniels, C. The small pulmonary lesion —surgical management. *Tr. Nat. Tuberc. A.*, 47: 226–231, 1951.
10. Meyer, A., Monod, O., Brunel, M. and Pesle, G. Segmental resection of lung. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 67: 262–269, 1951.
11. Conklin, W. S. and Westerberg, H. Segmental resection. *J. A. M. A.*, 146: 633–641, 1951.
12. Forsee, J. H., Jenipel, C. W. and Salzer, J. M. Recent advances in pulmonary resection. *Ann. Int. Med.*, 35: 417–431, 1951.
13. Kraan, J. K. Segmental resection in pulmonary tuberculosis. *Nederl. tijdschr. v. geneesk.*, 95: 3375–3381, 1951.
14. Marmet, A., Taubert, M., de Beaujeu, M., Ackerman, F. and Michemble, M. Small series of segmental resection in pulmonary tuberculosis in sanatorium environment. *Riv. Tuberc.*, 15: 999–1002, 1951.
15. Eerland, L. D. Results of resection therapy (segmental resection, lobectomy, pneumonectomy) in pulmonary tuberculosis during the period 1943–1951. Koninklijke Nederlandse Akademie von Wetenschappen. *Proceedings Series*, 54: 332–341, 464–468, 1951.
16. Monod, O., Meyer, A., Pesle, G., Coury, C., Bouridin, I., and Baton, D. Segmental resection in pulmonary tuberculosis. *Am. Rev. Tuberc.*, 16: 33, 1952.
17. Monod, O., Pesle, G. and Ghazi. Segmental resection in pulmonary tuberculosis. *J. de méd. de Bordeaux*, 129: 32–34, 1952.
18. Nuboer, T. F. Segmental resection in pulmonary tuberculosis. *Poumon*, 8: 41–50, 1952.
19. Mannes, P. Tuberculosis of inferior lobes and segmental resection. *Acta tuberc. belg.*, 43: 39–54, 1952.
20. Dor, Natalli, Du Cotell and Carcassone. Segmental resection: one case of resection of the apical-posterior segment in tuberculosis of the lung. *Marseille med.*, 89: 133–135, 1952.
21. Murphy, T. D. and Rayl, I. S. Segmental resection for pulmonary tuberculosis. *Dis. of Chest*, 23: 160–165, 1952.
22. Marmet, A., Taubert, M., de Beaujeu, M., Ernewein, F. and Petit, M. Indication for segmental resection in tuberculosis. *Lyon méd.*, 186: 280–284, 1952.
23. Zerbini, E. J. Segmental resection in the treatment of pulmonary tuberculosis. *Rev. paulista de med.*, 44: 247–256, 1952.
24. Marmet, A. Segmental resection for tuberculosis. *Strasbourg med.*, 3: 298–300, 1952.
25. DeRham, G. Indications for partial pulmonary resection in tuberculosis. *Rev. med. Suisse Rom.*, 72: 373–377, 1952.
26. Forster, E., Maier, A. and Keiling, L. Six cases of segmental resection for pulmonary tuberculosis. *Strasbourg med.*, 3: 681–689, 1952.
27. Storey, C. F. and Rothman, B. F. Segmental resection in the surgical treatment of pulmonary tuberculosis. *J. Internat. Coll. Surgeons*, 19: 53–68, 1953.
28. Overholt, R. D., Woods, R. M. and Wilson, N. G. Segmental resection in tuberculosis. *Dis. of Chest*, 23: 255–265, 1953.
29. Churchill, E. D. and Belsey, R. Segmental pneumonectomy in bronchiectasis. *Ann. Surg.*, 109: 481, 1939.
30. Blades, B. Conservation of lung tissue by partial lobectomy. *Ann. Surg.*, 118: 353, 1943.
31. Brock, R. C. Anatomy of the Bronchial Tree. London, 1946. Oxford University Press.
32. Clagett, O. J. and Deterling, R. A., Jr. Technique for segmental pulmonary resection with particular reference to lingulectomy. *J. Thoracic Surg.*, 15: 227, 1946.
33. Overholt, R. H. and Langer, L. New technique for pulmonary segmental resection. Its application in treatment of bronchiectasis. *Surg., Gynec. & Obst.*, 84: 257, 1947.
34. Medlar, E. M. Incidence of tuberculous pulmonary cavities in unexpected deaths investigated at necropsy. *Arch. Int. Med.*, 8: 407, 1947.
35. Medlar, E. M. and Sasano, K. J. A study of pathology of experimental pulmonary tuberculosis in the rabbit. *Am. Rev. Tuberc.*, 34: 456, 1936.
36. Dock, W. Apical localization of phthisis: its significance in treatment by prolonged rest in bed. *Am. Rev. Tuberc.*, 53: 297, 1946.
37. Daniels, C. F., Chamberlain, J. M. and Ford, J. M. Emergency resection for pulmonary tuberculosis (in press).
38. Klopstock, R. and Mathias, J. L. Lateral tomography as a guide in surgery for diseases of the lung. An Exhibit at New York Academy of Medicine, 22nd Graduate Fortnight, October, 1949.
39. Kane, I. Sectional Radiography of the Chest. New York, 1953. Springer Publishing Company, Inc.
40. Christie, R. V. Elastic properties of emphysematous lungs and their clinical significance. *J. Clin. Investigation*, 13: 279–294, 1934.
41. Cincotti, J. J. and Watson, T. R. Unpublished data.

Home Management of Pulmonary Tuberculosis and Other Forms

DONALD R. MCKAY, M.D., *Buffalo, New York*

FIFTY years ago when the death rate was 200 per 100,000 the treatment of pulmonary tuberculosis was carried on almost exclusively in the home of the patient. Fortunately the value of the sanatorium was recognized professionally and civically; and through this medium and the efforts of public health bodies and interested lay and professional groups, the death rate of the disease has steadily declined in this and many other countries. Although collapse therapy by pneumothorax, phrenic paralysis and thoracoplasty were widely used with striking beneficial results in individual cases, the mortality rate maintained a fairly steady curve until the advent of antimicrobials and improving methods of surgery after World War II. Since then the decline has been precipitous with no other factors to explain it other than a generally good economic status of our people which, however, antedated the sharp decline.

During the past seven or eight years we have been groping by research and practical application for satisfactory treatment formulas. Now, although more effective drugs will be developed we hope, more general agreement on definitive treatment is being achieved; this even though therapy has been a rapidly changing affair having definite trends toward more all inclusive use of chemotherapy, less rigid rest regimes for those without constitutional symptoms and under drug therapy, fewer collapse procedures and more excisions of caseous and necrotic lesions. Future therapeutic regimens may be greatly broadened if we accept for treatment tuberculin converters,[1] especially from homes of tuberculous families, medical and dental students, student and graduate nurses and other hospital personnel having patient contact. Lincoln[2] in a recent article showed that primary tuberculosis without calcification in children can be most effectively treated by drug combinations including INH, recent mortality rate being 1.5 as against 21.5 in the prespecific therapy period before 1946. Apparently INH prevents the development of the complications of primary tuberculosis, especially meningitis. The tuberculin test is once more becoming a very valuable procedure and should be used more freely by pediatricians in contact and suspect cases. Its value in the aforementioned contact groups is unquestionable. In our experience the hospital personnel converters are a group most likely to develop serious disease. Either a program of BCG vaccination or prompt treatment of primary lesions should be carried out.

So far four drugs are of general practical value. Streptomycin and dihydrostreptomycin have been shown to be mainly bacteriostatic and extracellular in action,[3] PAS or Sod. PAS to have the same reaction to a lesser degree; and when used with INH, SM or DHSM delays the emergence of resistant forms. INH has been shown to have a good intracellular effect as well, which may in many cases result in a dormant organism incapable of infecting a guinea pig or growing in culture. However, recent observations[4] indicate that many "healed" lesions will produce viable organisms. Variations in viability in different lesions from the same patient suggest emergence of resistant forms *in vitro* is not the sole criterion for discontinuing therapy or evaluating the need for surgical procedures. Viomycin and terramycin® have been substituted where untoward reactions to other drugs developed. The results achieved have not been very convincing.

Although the death rate has declined sharply, new cases of tuberculosis have not declined proportionately. Most health department registers contain almost as many names as ever. This means that for some time we shall have a large reservoir of cases calling for management and treatment. It has long been established that tuberculosis is a disease which tends to recur again and again in some individuals,

especially in those untreated with drugs. How much antimicrobial drugs prevent recurrences has not yet been satisfactorily established.[5] At any rate, it would seem that a person developing tuberculosis now has a better chance of surviving a much longer period than a similar individual in the pre-antimicrobial era. Such survival along with better case-finding methods tends to swell the numbers of reported cases, and calls for continued supervision on the part of hospitals, clinics or physicians. Our County of approximately one million persons has available institutional beds for about 800 persons. The Tuberculosis Register contains the names of over 4,000 persons. I believe this situation is fairly representative of the average community. What happens to the 3,000 odd patients who are not in a sanatorium or hospital? Obviously most of them need not be there; they have received "maximum hospital benefits" or have had minimal disease which did not appear to require institutional care; or for social, economic or psychiatric reasons failed to cooperate with their hospital regimen. Persons in the later decades of life find it most difficult to feel happy and contented for prolonged hospital periods, preferring to be at home. Since tuberculosis finds most of its victims in areas of poor social and economic status, it is not surprising that ignorance, comparative illiteracy and alcoholism make it difficult for Health Department personnel to achieve desired results. Although a large number of these persons may be inactive, there is a considerable number who require constant observation and therapy in outpatient treatment clinics or under the direct supervision of their physicians.

What sort of supervision and treatment have we to offer today?[6] Close liaison with Health Department and Public Welfare officials as well as private social organizations is essential for those unable to maintain a good standard of living. When necessary, adequate housing, clothing and food must be provided in addition to clinic services. More fortunate persons may prefer physicians of their own choosing to supervise their treatment, but close association with Health Department officials is still essential for many reasons, particularly the periodic survey of contacts. The physician undertaking such supervision must be assured that his patient has good housing in which practical isolation technics can be carried out, that adequate diet will be provided and that an adequate rest regimen (not necessarily continuous bed rest) may be maintained, in addition to assurance that antimicrobial therapy will be properly administered. Supervision must also be carried out mindful of surgical possibilities whether the lesion be pulmonary, genitourinary, orthopedic, etc. A drug therapy program develops closer relationship between physician and patient so that advice as to return to sanatorium or hospital, the need of surgery, etc., is often more readily accepted.

TABLE 1
EIGHTY-SIX PATIENTS

Decade	No. of Cases	Sex		Type of Disease			
		Male	Female	Pulmonary I	Pulmonary II	Pulmonary III	Other
0–9	3	..	3	..	..	..	3
10–19	1	..	1	1	..	..	..
20–29	11	4	7	3	4	4	..
30–39	18	6	12	3	2	7	6
40–49	24	9	15	4	3	13	4
50–59	15	10	5	2	6	3	4
60–69	11	8	3	2	5	4	..
70 and over	3	3	..	1	..	2	..
Total	86	40	46	16	20	33	17

An analysis of eighty-six unselected patients who are receiving antimicrobials or have received them for two or more months during the past five years indicates that fifty-three patients were over forty years of age. Seventy-one patients had varying periods of sanatorium or hospital care; thirteen had home administration of drugs preoperatively and twenty-four were treated postoperatively. Seventeen patients were treated for non-pulmonary lesions; sixteen, twenty and thirty-three were minimal, moderately advanced and far advanced lesions, respectively. Many of these cases represent efforts undertaken with other specialists such as chest surgeons, orthopedists and urologists. (Table 1.)

TREATMENT OF MINIMAL TUBERCULOSIS

Sixteen patients were or are being treated, eleven of whom spent varying periods in a hospital or sanatorium. Treatment regimens in most instances supplemented sanatorium programs. All three drugs were administered in eight cases: streptomycin and INH in four, streptomycin and PAS in three, and INH and

PAS in one. Treatment periods have varied from two months (continuing) to twenty-six months, with an average duration of nine months. Dosage in most cases was streptomycin or dihydrostreptomycin or a combination of the two, 1 gm. twice weekly; INH 300 mg. per day, and PAS 8 to 12 gm. daily. Recently the sodium salt of PAS has been found to be less irritating to the gastrointestinal system.

Results are difficult to evaluate since minimal lesions often respond well in their earlier phases to rest, diet, etc. We have, however, been impressed by the rapid disappearance of toxic symptoms and the rapid conversion of sputum or gastric washings under drug therapy. Patients can be treated on a semi-ambulant basis and most were able to return to work or household duties at an earlier period. Seven patients are inactive at present and the remainder are all improved or have arrested conditions. No complications of any importance developed either as a result of the disease or due to drugs. With the exception of four who have been under treatment for less than six months, the majority of the patients are actively engaged in their regular activities with restrictions on competitive games, overtime work and the like.

If we discard our fears of bacterial resistance and recognize that meningitis does not occur in INH-treated patients, that converters in association with tuberculous patients develop the disease at a rapid rate and that young children have an alarming death rate from primary tuberculosis, it would seem apparent that early and adequate use of drugs is imperative. The long-term outlook for active untreated minimal tuberculosis is none too good. Mitchell in a twenty-year follow-up on Trudeau Sanatorium patients from 1927 to 1946 reported that 27.6 per cent of "minimals" progressed to advanced disease with resultant periods of morbidity, economic loss and a 5 per cent mortality.[7]

Only the future can tell us about the efficiency of our present programs. If it is true that chemotherapy (INH) can attenuate the tubercle bacillus *in vivo*, it would seem logical to continue therapy for prolonged periods, not now clearly defined.[8] So far we have seen little evidence of progression in any patient under treatment. The present tendency to treat each patient for about six months after disappearance of symptoms, x-ray stability and negative culture on sputum or gastric washings may be indefinitely prolonged. Perhaps we are reaching a situation somewhat analogous to the treatment of malaria. Many recent studies have not resulted in a categoric treatment regimen. Recent observations suggest that INH alone may be a satisfactory agent particularly in home-treated cases because of effectiveness, lack of complications and low cost.[6] However, until treatment criterion becomes more sharply delineated, I am inclined to agree with Waring;[1] hit hard and long with available combinations, preferably SM, INH and PAS. If we believe such a program is indicated in pneumonic, miliary or meningitic lesions, and keeping in mind recurrence rate in untreated cases, it would seem wise to put out the early fires as effectively as possible with the same weapons. How much surgery is necessary in these cases at the present time evokes wide differences of opinion.

TREATMENT OF MODERATELY ADVANCED PULMONARY TUBERCULOSIS

Of twenty patients in this group fourteen had some hospital or sanatorium experience. The other six for various reasons were treated exclusively at home. Five had surgical resections. Of the resection patients four are considered inactive and are working. Seven others are inactive and the remainder improved. The group received triple drugs in eleven instances and either SM and PAS or INH or PAS in the remainder, except one who was treated four months on INH alone. Duration of home treatment averaged twelve months to date and many are being continued. The results so far are very comparable to the group of early pulmonary tuberculosis. However, we believe, in spite of present negative sputa or gastric washings, that some of these patients may eventually need excisional surgery. It is in this group that the physician or conference group finds the greatest difficulty in honestly evaluating patients, since even with lordotic films and planograms it is often difficult to distinguish between residual small cavities and annular shadows caused by the pulmonary infiltrates.[4] Certainly a fair percentage of this group should have the more extensive portions of their disease eliminated by surgery. This, with long-term drug therapy, should materially reduce the recurrence rate.

TREATMENT OF FAR ADVANCED TUBERCULOSIS

This group presents the greatest problems and greatest frustrations. Although case finding has improved, unfortunately too many patients are still diagnosed when widespread pneumonic, exudative and cavitary disease is present. To these we add the large number of chronic patients who have had recurrences of their lesion whether or not collapse therapy in one form or other had been used. In our series of thirty-three patients thirty-one had previous hospital or sanatorium care. Two patients have died (one age seventy-five with evidence of cor pulmonale and one postoperatively); twelve are unchanged or worse and nineteen are inactive or improved. One of the latter has diabetes mellitus controlled. Three are working at their usual employment; eight of the surgical patients have been definitely improved or rendered inactive. Fifteen have received triple drugs in their home management, and the others a double combination for an average of sixteen months. The series is too small to draw any definite conclusions as to superiority of any regimen except that observations on these patients and others treated in the E. J. Meyer Hospital suggest that clinically, roentgenologically and bacteriologically those who received triple drugs reacted more favorably than the others. Striking results were obtained in some individual patients who had severe complications. Where possible and indicated, excisional surgery is a health-restoring procedure. Where too little pulmonary reserve is left, pneumoperitoneum or thoracoplasty may be wisely chosen as "holding" procedures. Clinical observation of the patient's response to exercise together with breathing function studies, knowledge of cardiac status, etc., are useful guides as to the type of interference which will be tolerated, or may result in a decision to continue antimicrobial therapy alone.

TREATMENT OF EXTRAPULMONARY LESIONS

The physician interested in tuberculosis is often consulted relative to this type of tuberculosis. Although the diagnosis of salpingitis and peritonitis is one most often made on exploratory laparotomy or in the pathologic laboratory, these conditions in common with kidney, lymph gland, bone and joint lesions respond most favorably to pre- and postoperative antimicrobial therapy. In a small series of seventeen cases which included two kidney lesions, six gland, two peritonitis, three salpingitis, one epididymitis, one knee joint and one ankle joint all recovered or were definitely improved. Two children who ordinarily would have had ankylosis of joints were restored to almost normal range of motion under drug therapy only. Drugs, dosage and duration of treatment is similar to pulmonary lesions.

TOXIC SYMPTOMS

On the dosages used there has been little vertigo or apparent hearing loss due to SM or DHSM. One patient felt "dopey," mildly depressed and a trifle unsteady. Mild reactions to INH were rare. One patient who was previously highly nervous recovered from a severe anxiety state in about four months. Mild dermatitis occurred in two cases. Severe complications such as convulsions, hepatitis, psychosis and peripheral neuritis were not encountered although recent reports indicate the drug is not without severe complications.[9,10] PAS in most of the patients at some time or other becomes an objectionable drug due to gastrointestinal irritation and diarrhea. Occasionally it was necessary to stop the drug for a few days and resume on reduced dosage. Severe skin reactions, toxic hepatitis or allergic reactions[11] were not observed.

SUMMARY

The home management of tuberculosis is discussed by illustrating experiences with eighty-six patients cared for by office practice. Treatment has been integrated with sanatorium or hospital programs in most instances. Since large numbers of tuberculous patients must of necessity be observed outside of hospital or sanatorium, it seems highly practical that physicians interested in this disease should take an active part in the therapy of an increasing number of persons as antimicrobial indications are broadened.

Close liaison with health department officials is highly desirable. The inclusion of surgical procedures in many cases may be health restoring. It is suggested that long-continued use of drugs may sharply reduce the recurrence rate.

REFERENCES

1. Waring, J. J. The current treatment of pulmonary tuberculosis. *Dis. of Chest*, 25: 361, 1954.
2. Lincoln, E. The effect of antimicrobial therapy on the prognosis of primary tuberculosis in children. *Am. Rev. Tuberc.*, 69: 682, 1954.
3. Mackaness, G. B. and Smith, N. The bacteriocidal action of isoniazid, streptomycin and terramycin on extracellular and intracellular tubercle bacilli. *Am. Rev. Tuberc.*, 67: 322, 1953.
4. Hobby, G. L., Auerbach, O., Lenert, T. F., Small, M. J. and Comer, J. V. The late emergence of M. tuberculosis in liquid cultures of pulmonary lesions resected from humans. *Am. Rev. Tuberc.*, 70: 191, 1954.
5. Mitchell, R. S. Early results of prolonged streptomycin-PAS treatment of pulmonary tuberculosis. *Am. Int. Med.*, 41: 282, 1954.
6. Robins, A. B., Abeles, H., Chaves, A. D., Aronsohn, M. H., Breuer, J., Widelock, D. and Peizer, L. The unhospitalized tuberculosis patient. *Am. Rev. Tuberc.*, 69: 26, 1954.
7. Mitchell, R. S. Late results of modified bed rest in active uncomplicated minimal pulmonary tuberculosis. *Am. Rev. Tuberc.*, 67: 401, 1953.
8. Dooneief, A. S. and Hite, K. E. Indefinitely prolonged chemotherapy for tuberculosis, preliminary report. *Am. Rev. Tuberc.*, 70: 219, 1954.
9. Vysniauskas, C. and Brueckner, H. H. Severe reactions of the central nervous system following isoniazid treatment. *Am. Rev. Tuberc.*, 69: 759, 1954.
10. Payne, H. M., Hackney, R. L., Jr., Clark, E. A. and Johnson, P. C. Clinical observations on the use of isoniazid in tuberculosis. *Dis. of Chest*, 25: 611, 1954.
11. Korst, D. R. Severe reactions to para-aminosalicylic acid: a case report and brief review of literature. *Ann. Int. Med.*, 40: 1011–1016, 1954.

Present Status of Pneumotherapy in the Management of Pulmonary Tuberculosis

JAMES H. CULLEN, M.D., *Albany, New York*

THOSE forms of treatment that indirectly attack the cause of a disease usually wax and wane in popularity, whereas specific therapy, such as antisera, chemotherapy or hormones which eliminate or correct the disease process, remain constantly in use changing only in details of administration. Pneumothorax and pneumoperitoneum are certainly examples of indirect therapy which attempt to correct the effects of the tissue destruction caused by the tubercle bacillus but do not attack the organism directly. Their popularity has varied considerably from time to time and even in treatment centers geographically close together there often is a marked difference in the frequency of their use.

The purpose desired in applying pneumotherapy, as in any collapse procedure, is relaxation of the diseased lung parenchyma. As a result of the relaxation and decrease in the size of the diseased area of the lung, cavity closure and conversion of the sputum to negative are facilitated. Pulmonary hemorrhage from a tuberculosis cavity is often controlled in the same manner. In common with all other forms of treatment in tuberculosis: the more recent the disease, the less its extent; the smaller the cavities, the more likely a good result will be obtained.

The popularity of pneumothorax and pneumoperitoneum in the New York Metropolitan area between 1945 and 1952 is shown in Figure 1, taken from a study by Lowell.[1] This shows the decline in pneumothorax refills after 1947 and the concomitant increase in pneumoperitoneum. Over the same period but including 1953, the number of pneumothoraces induced follows a similar curve but the fall starts two years later, the peak of 1,200 initial pneumothoraces being reached in 1949 and falling to 277 in 1953. During this same period thoracoplasties reached a height of 927 in 1949, and in 1953, 317 were done. Lobectomies and pneumonectomies have remained constant from 1951 through 1953 (415 and 387). During this period from 1945 to 1953 the number of patients under treatment in the reporting hospitals remained fairly constant, so the number of procedures done from year to year can be fairly compared.

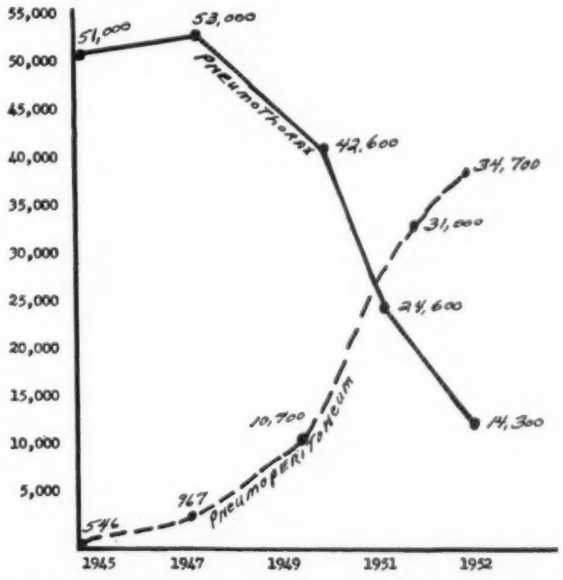


FIG. 1. Yearly number of pneumothorax and pneumoperitoneum refills in Metropolitan New York. (After A. M. Lowell of the New York Tuberculosis and Health Association.)

The decline in the use of artificial pneumothorax in the treatment of tuberculosis seems to have occurred coincidental with the development of other methods of treatment, and with an increased awareness of the adverse long-term effect of its complications such as empyema, unexpandable lung and the loss of pulmonary function. The results, in terms of sputum conversion from positive to negative, of some collapse and resection procedures are shown in Figure 2.

The first bar represents the 47 per cent conversion obtained in cavitary disease with pneumoperitoneum as reported by Trimble

et al.[2] There was a one- to ten-year follow-up, although in 84 per cent of the cases pneumoperitoneum was initiated in the last five years of the study. The next bar shows the 57 per cent sputum conversion in the first year of therapeutic pneumothorax as reported by Mitchell.[3]

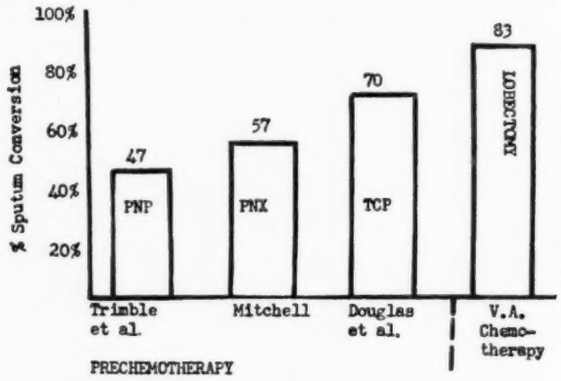


FIG. 2. Comparative results of treatment.

However, 17 per cent of these reactivated their disease in the next ten years, and ten to twenty years after induction there were only 39 per cent good results. In the third bar are the 70 per cent sputum conversions following thoracoplasty reported by Douglas and Bosworth.[4] In a ten-year follow-up there were 12 per cent relapses. The first three groups of patients were all treated in the prechemotherapy era, whereas the final bar represents the 83 per cent conversion occurring within eight months after lobectomy done during the course of combined chemotherapy as reported by the Thirteenth Chemotherapy Conference.[5] These patients were operated upon in various hospitals all over the country and it probably gives a good representation of the immediate results to be expected in patients suitable for a resection such as lobectomy.

As is seen in Figure 2, the immediate results of pneumothorax are very little better than pneumoperitoneum and are inferior to those of thoracoplasty. If only primary thoracoplasties (thoracoplasties performed on patients who never had any other collapse procedure) are considered, 75 to 85 per cent sputum conversion is to be expected, which increases still further the disparity between the results of thoracoplasty and pneumothorax. In addition to this there are in 80 per cent or more of pneumothoraces adhesions which should be cut by pneumonolysis in order to obtain a good selective collapse as has been frequently reported, most recently by Birath[6] of Sweden.

Another reason for the decline in popularity of pneumothorax is the high incidence of serious complications, especially in reports of long-term studies. Figure 3 presents the incidence of the complications of pneumothorax, lobectomy and pneumoperitoneum. The first

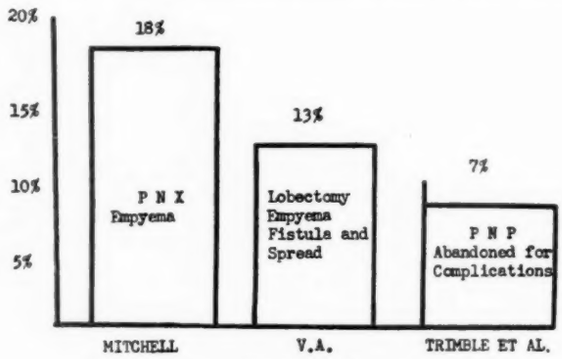


FIG. 3. Complications of treatment.

bar represents just one complication of pneumothorax, namely empyema, which was reported by Mitchell[7] to occur in 18 per cent of the cases he studied. Even so, this one complication was more frequent than the sum total of the major complications of lobectomy of 13 per cent, as reported by the Thirteenth Chemotherapy Conference.[5] This 13 per cent incidence of complications is higher than the true figure as many patients had more than one complication, such as fistula plus empyema, but these were each counted separately. Pneumoperitoneum has the least complications. In the series of Trimble et al.[2] 7 per cent were discontinued because of complications. Again it is seen that pneumothorax is in a less favorable position than other procedures.

That significant pleural effusion is not prevented by chemotherapy given before and after the induction of pneumothorax is shown in the report of Birath.[6] Without prior chemotherapy 27 per cent of his patients developed fluid in the first six months of pneumothorax which lasted for two months or more, whereas when combined chemotherapy was given before and during pneumothorax 7 per cent developed an effusion that persisted for over two months. There were 3 per cent empyemas in the first group, none in the second. As these pneumothoraces are maintained, the incidence of fluid can be expected to increase still further.

Finally, it has been shown time and again that the maintenance of pneumothorax is associated with a definite and often consider-

able loss of pulmonary function. This loss is more closely associated with the amount of pleural and diaphragmatic involvement than with the loss of pulmonary parenchyma as a result of disease.

It is probably the general recognition of the fact that the long-term results are not nearly as good as the immediate results, and the appreciation of the seriousness and frequency of complications that has led to the decline in the use of pneumothorax. The improved surgical results and use of chemotherapy have also been important factors in its fall from favor in the treatment of tuberculosis. At the present time one cannot predict the place that pneumothorax will have in the future in the treatment of pulmonary tuberculosis. We are now in a wave of reaction against it but eventually the pendulum may swing back to its more frequent use, although I do not believe it will ever again be used as extensively as it was in the 1930's and early 1940's. A good long-term study, preferably controlled, of its use combined with chemotherapy is badly needed to determine its place in the present day therapy of tuberculosis. However, the studies of the prechemotherapy era seem to indicate that if other measures can control the disease, the long-term results will be better and complications will be less than they would be with pneumothorax. The only undisputed indication for pneumothorax at present is pulmonary hemorrhage uncontrollable by other means where it sometimes stops the bleeding.

As was shown in Figure 1, the popularity of pneumoperitoneum has increased as that of pneumothorax declined. The combined total of pneumothorax and pneumoperitoneum refills of 49,000 in 1952 almost reaches the peak of 54,000 refills in 1947. According to Lowell[1] in 1953 a total of 1,000 pneumothoraces and pneumoperitoneums (277 and 729, respectively) were induced. In the peak years of 1947 and 1949, 1,200 pneumothoraces were started. From this it can be seen that pneumotherapy is almost as popular as ever.

It is seen in Figure 2 that in the prechemotherapy era the immediate sputum conversion rate following pneumoperitoneum is not as great as that with pneumothorax, and this has been the general experience and is not limited to the studies of Trimble et al.[2] and Mitchell.[3] Of course, exact comparisons between different studies cannot be made because of differences in patient characteristics, duration and thoroughness of follow-up, and concomitant therapy available.

Since sputum conversion is a little less frequent than with pneumothorax, it is probably the very low incidence of distressing or serious complications, as shown in Figure 3, which tipped the balance so much in favor of pneumoperitoneum at the expense of pneumothorax. Bobrowitz[8] has listed all the complications of pneumoperitoneum associated with 24,750 refills in 561 patients. Weight loss was by far the most common and occurred in 62 per cent of the patients. Although peritoneal fluid occurred in 4.7 per cent, it was a cause of termination of pneumoperitoneum in only 1.7 per cent. Pain early in the course of pneumoperitoneum was a common occurrence but usually subsided as the treatment was continued. Hernia occasionally occurred during treatment. Acute appendicitis was usually a more serious disease than in those without pneumoperitoneum because of atypical signs and its failure to localize. The two most dangerous complications were pneumothorax often associated with mediastinal emphysema, and air embolism. They had just two instances of each of these.

The location of the cavity in the lung does not effect the incidence of cavity closure and sputum conversion as was shown in the report of Trimble et al.[2] The results of pneumoperitoneum are much more influenced by cavity size and duration of disease than the position of the cavity. The pressure changes and relaxation of lung parenchyma, as a result of the elevation of the diaphragms and reduction in thoracic volume, are transmitted equally throughout the pulmonary tissue unless restrained by adhesions. The larger the cavity and the more fibrotic the disease, the less are the chances of good result.

Early in the use of pneumoperitoneum a phrenic crush was frequently done as an associated procedure sometimes before and sometimes after the induction of the pneumoperitoneum. It was thought that by paralyzing the diaphragm on the more involved side the additional diaphragmatic elevation would improve the chances of cavity closure. However, in the studies of Trimble et al.[2] and Mitchell et al.[9] the incidence of good results was no greater in those patients receiving combined pneumoperitoneum and phrenic crush than in those who received pneumoperitoneum alone. As is

well known, the loss of diaphragmatic motion causes a loss of one-quarter to one-third of the ventilatory function of the involved side. In addition the force of coughing is interfered with and this becomes especially important if major thoracic surgery becomes necessary. All too often a "temporary phrenic crush" leads to permanent total or partial diaphragmatic paralysis, especially if the procedure is repeated. In the absence of pneumoperitoneum Mitchell[10] found 6 per cent total paralysis and 26 per cent partial after a single phrenic crush, and this increased to 11 and 35 per cent, respectively, when multiple operations were performed. In the presence of pneumoperitoneum Mitchell et al.[9] found 42 per cent total and 9.5 per cent partial paralysis, one to four years after phrenic crush had been done. It is because of the high incidence of permanent diaphragmatic paralysis, with its attendant disadvantages, and the fact that equally good results with pneumoperitoneum are obtained without it that the combined procedures are used much less frequently than formerly.

Although it remains to be conclusively demonstrated, there are some studies which indicate that pneumoperitoneum instituted early (first two months) in the course of long-term combined chemotherapy improves the results. In a report by Brinkman et al.[11] the authors found that pneumoperitoneum started in the first month of chemotherapy increased the incidence of cavity closure at eight months to 86 per cent, whereas in similar cases treated with chemotherapy without pneumoperitoneum cavity closure occurred in 62 per cent. Sputum conversion showed a similar difference of 81 and 67 per cent, respectively, in favor of the addition of pneumoperitoneum. The differences in the two groups of cases were especially marked when the original cavities were 2 cm. or over in size. Moyer and Schwartz[12] found that pneumoperitoneum added to combined chemotherapy increased the incidence of cavity closure but not of sputum conversion. In neither of these studies were concurrent controls used selected in a random manner as to those treated with and without pneumoperitoneum. Because of this one might question the differences found as representing inapparent, unconscious bias in the selection of cases for the group receiving or not receiving pneumoperitoneum to their respective advantage or disadvantage. The Veterans Administration—Army—Navy Chemotherapy Cooperative Study has embarked on a controlled study with random selection of patients into groups receiving and not receiving pneumoperitoneum, but the results have not been reported as yet.

Since these studies indicate that in cavitary disease chemotherapy and pneumoperitoneum combined seem to give better results than chemotherapy alone, serious consideration has to be given to using both procedures in all cases with cavity especially if over 2 cm. in size. The experience at Trudeau[11] suggests that the results are much better if the pneumoperitoneum is instituted soon after the introduction of chemotherapy rather than later. Ordinarily one would reserve pneumoperitoneum for anticipated chemotherapy failures or individuals receiving chemotherapy who had not obtained cavity closure and sputum conversion by the fourth to sixth month. Using pneumoperitoneum in most cases with cavitary disease is not without its disadvantages in spite of the low incidence of serious complications with this procedure. As was shown in the report by Bobrowitz,[8] 62 per cent of the patients receiving pneumoperitoneum lost weight, and in addition, it is moderately uncomfortable. It requires refills at about ten-day intervals for a year or more, which chain the patient to their doctor and interfere with movement from place to place. In view of these minor but distressing disadvantages and our reluctance to treat all patients in the same routine manner, it is obvious that there is an urgent need for reasonably accurate criteria that will detect those cases in which chemotherapy alone will fail, and which would be helped by combined chemotherapy and pneumoperitoneum. Until such information is available, it is recommended that pneumoperitoneum be instituted in cases in which it is anticipated the chemotherapy alone will fail (because of cavity size, more chronic disease, older age patients, extent of disease). It is also important to decide early during a course of chemotherapy which cases are not responding rapidly as to cavity closure and sputum conversion and in these start pneumoperitoneum without delay. Pneumoperitoneum is especially needed in those patients who are not suitable for surgical procedures, such as thorocoplasty and resection. Pneumoperitoneum is also often helpful in controlling pulmonary hemorrhage.

SUMMARY

1. The reasons for the decline in popularity of therapeutic pneumothorax such as its pleural complications and its effect on pulmonary function are discussed.

2. The need for re-evaluation of pneumothorax combined with chemotherapy is recognized but it must await reports of long-term results.

3. Pneumoperitoneum is replacing pneumothorax in popularity and is needed in anticipated or demonstrated chemotherapeutic failures, especially if thoracic surgery is not applicable.

4. The use of pneumoperitoneum early in the course of chemotherapy in the presence of cavitary disease is discussed.

REFERENCES

1. Lowell, A. M. Tuberculosis in New York City 1953, p. 18. New York, 1954. New York Tuberculosis & Health Assoc.
2. Trimble, H. G., Eaton, J. L., Crenshaw, G. L. and Gourley, I. Pneumoperitoneum in the treatment of pulmonary tuberculosis. *Am. Rev. Tuberc.*, 52: 433, 1948.
3. Mitchell, R. S. Artificial pneumothorax: a statistical analysis of 557 cases initiated 1930–1939 and followed in 1949. I. *Am. Rev. Tuberc.*, 64: 1, 1951.
4. Douglas, R. and Bosworth, E. B. The after-history of pulmonary tuberculosis. II. Thoracoplasty: ten-year follow-up. *Am. Rev. Tuberc.*, 69: 930, 1954.
5. Transactions of the Thirteenth Conference on the Chemotherapy of Tuberculosis. Veterans Administration—Army—Navy, 1954.
6. Birath, D. G. The initial period of artificial pneumothorax. *Dis. of Chest*, 24: 245, 1953.
7. Mitchell, R. S. Artificial pneumothorax: a statistical analysis of 557 cases initiated 1930–1939 and followed in 1949. IV. Incidence, mortality, and factors associated with complicating tuberculous empyema. *Am. Rev. Tuberc.*, 64: 127, 1951.
8. Bobrowitz, I. D. Complications of pneumoperitoneum therapy. *Dis. of Chest*, 24: 82, 1953.
9. Mitchell, R. S., Hiatt, J. S., McCain, P. P., Eason, H. F. and Thomas, C. D. "Pneumoperitoneum in the treatment of pulmonary tuberculosis. *Am. Rev. Tuberc.*, 50: 306, 1947.
10. Mitchell, R. S. Phrenic nerve interruption in the treatment of pulmonary tuberculosis. II. Complications and sequelae of phreniclasis. *Am. Rev. Tuberc.*, 60: 168, 1949.
11. Brinkman, G. L., Raleigh, J. and Mitchell, R. S. The use of pneumoperitoneum as an adjunct to the prolonged streptomycin-para-amino salicylic acid treatment of pulmonary tuberculosis. *Am. Rev. Tuberc.*, 69: 963, 1954.
12. Moyer, R. E. and Schwartz, W. S. Results of addition of pneumoperitoneum to long-term chemotherapy. Transactions of the Thirteenth Conference on the Chemotherapy of Tuberculosis. Veterans Administration—Army—Navy, 1954.

Hemangioendothelioma of Palate, with Wide Surgical Removal and Immediate Skin Graft

PINCUS SHERMAN, M.D., D.D.S. AND CLARENCE M. CALMAN, B.S., D.D.S., *New York, New York*

HEMANGIOENDOTHELIOMA is a rare type of angiomatous tumor. The term was first used by Mallory in 1908 to describe this malignant vascular tumor in which the endothelial cell is responsible for the aggressive growth and metastatic properties of the lesion.[1] Drucker[2] reports only eight cases treated at Bellevue Hospital in twenty-two years. Cheyne and Silberstein,[3] in their review of the literature, stress the infrequency of this lesion especially in the oral cavity.

Three types of treatment generally are recommended for this type of lesion.[2] They are surgery, irradiation and a combination of both. In view of the circumscribed nature of the lesion presented herein, it was decided that all visibly affected tissue would be removed. This would denude a large area of palatal bone. In order to cover this exposed bony area effectively and reduce postoperative complications of pain, infection and delayed healing, an immediate split-thickness skin graft was planned.

CASE REPORT

R. R., a fifty year old Puerto Rican man, presented himself to the New York City Hospital Outpatient Department, complaining of a painless growth on his palate which interfered with the proper seating of his denture.

The patient stated that he had had gonorrhea and syphilis dating back twenty-five years which had been treated with arsenicals. At that time he was discharged as cured. In 1946 it was discovered he had diabetes and he has been under treatment with insulin ever since. In 1947 a pedunculated lesion of the abdomen was removed surgically at City Hospital. Histopathologic diagnosis of this lesion was "inflammatory granuloma." On routine examination in December of the same year the Mazzini test was doubtful and the Wassermann test, 1 +.

In April, 1952, the patient was seen at the Outpatient Department of New York City Hospital, complaining of two polypoid growths. One was at the right retromolar triangle of the mandible. The other was in the tuberosity of the right maxilla. These were removed *in toto*. The histopathologic report of the maxillary lesion was "polyp with acute and chronic inflammation." The polyp of the mandible was diagnosed histopathologically as "rhabdomyosarcoma." All attempts to recall the patient at that time were futile.

In November, 1952, he reappeared at the Clinic with his present complaint and was immediately hospitalized.

One month prior to admission the patient had noticed a slight swelling on the palate in the vicinity of the right second molar. This was painless, but it bled on the slightest trauma and interfered with the retention of his upper denture. The mass rapidly increased in size to its present proportion.

Physical examination revealed a well developed, well nourished man, not acutely ill with normal temperature, pulse and respiration. There were no gross abnormalities and the site of the excised abdominal mass was completely healed.

Local examination of the oral cavity revealed that in the upper right posterior palatal region there was a greyish white pedunculated cauliflower-like lesion with a broad sessile base. (Figs. 1 and 2.) It was 2.5 cm. in length and 2 cm. wide. The lesion was raised approximately 1 cm. from its base. On palpation it was painless and soft. The underlying tissue was found to be extremely raw and it bled easily and profusely. The mucous membrane extend-

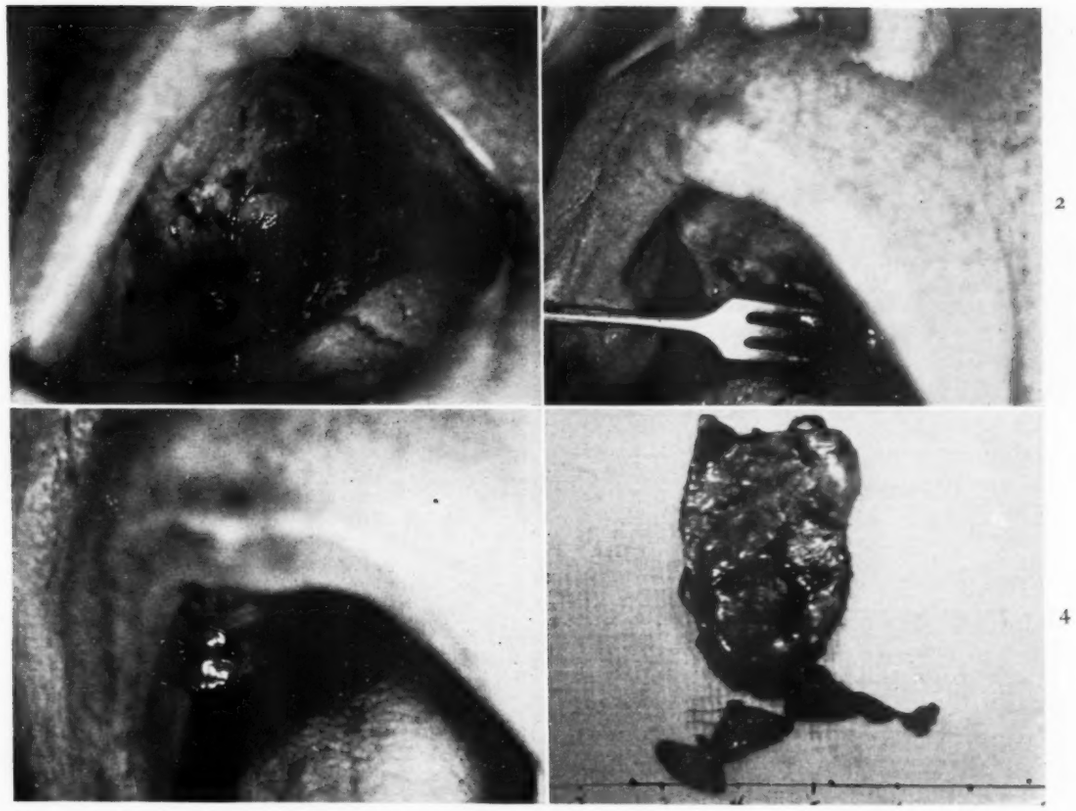


FIG. 1. Lesion *in situ*. FIG. 2. Lesion retracted. FIG. 3. Site of previous surgery. FIG. 4. Lesion removed.

ing anteriorly and laterally almost to the alveolar ridge was hyperemic and intermingled with whitish areas throughout. Towards the midline, just anterior to the main lesion, the normal mucous membrane was interspersed with discrete bluish discolorations. No lymphadenopathy was present. The sites of previous surgery were completely healed and of no clinical interest. (Fig. 3.)

X-rays of the mandible, maxilla and chest were negative. Mazzini test was negative; red blood count, 4,340,000; hemoglobin, 17.5 gm.; white blood count, 7,400; polymorphonuclear, 42 per cent (4 per cent stab forms); lymphocytes, 52 per cent; monocytes, 2 per cent; eosinophils, 4 per cent; no abnormal forms found. Blood sugar was 222 mg. per cent; blood urea nitrogen, 20; alkaline phosphatase, 2.9. Liver function tests: cholesterol, 258; esters, 176; icteric index, 8.0; albumin, 5.1; globulin, 3.9; thymol time, 13.0 units.

Blood sugar tests were repeated and the operation was planned when the patient was in the best physical condition. On December 3, 1952, the entire palatal area was anesthetized with 2 per cent procaine injected into both posterior palatine canals and the anterior palatine foramen. The right mucobuccal fold was infiltrated. Due to the extent of the lesion the incision was made in the midline of the palate $2\frac{1}{2}$ cm. posterior to the incisive foramen, and carried posteriorly along the midline to a point 2 cm. posterior to the junction of the hard and soft palate. The incision was then extended laterally on the right side along the soft palate to the alveolar ridge and then along the ridge anteriorly to a point 2 cm. distal to the incisive foramen.

The tissue was completely removed from bone on the hard palate and from the musculature on the soft palate. This tissue contained the lesion and all the abnormal mucous membrane as previously described. (Fig. 4.) The posterior and anterior palatine vessels were ligated with No. 000 silk. All bleeding was arrested. The underlying bone and soft tissue appeared grossly normal.

An area 14 by 12 cm. was infiltrated with 2 per cent procaine on the ventral surface of the left thigh. A split-thickness skin graft was removed freehand, approximately 3 cm. in width and 12 cm. in length. The graft was

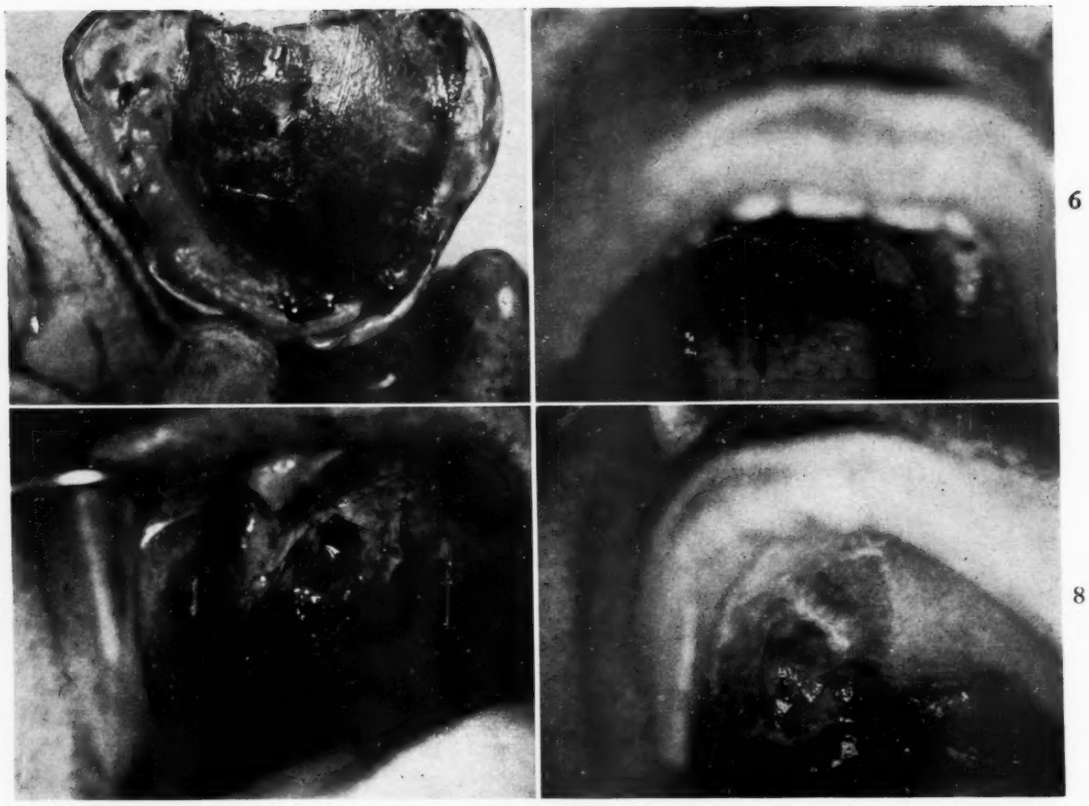


FIG. 5. Split-thickness graft applied to denture. FIG. 6. Denture in place in mouth. FIG. 7. Area after removal of stent. FIG. 8. Area completely healed.

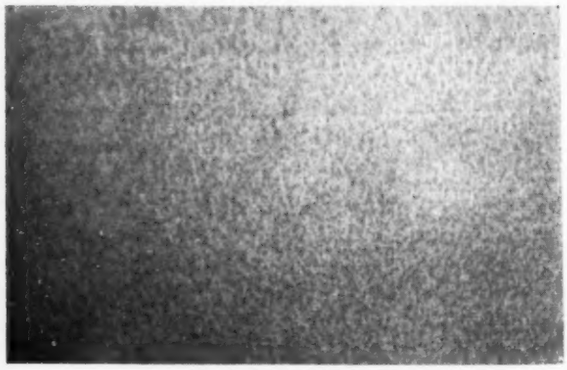


FIG. 9. Pathologic slide. (× 100.)

backed with petrolatum gauze, and the donor site covered with one layer of mesh gauze. The raw surface of the split-thickness skin graft was bathed with topical thrombin.

The graft was placed on the patient's denture so that the raw surface would be in contact with the prepared recipient site on the palate. (Fig. 5.) To provide peripheral seal for retention of the denture, gelatine foam sponge was molded on the posterior edge of the denture. The plate, acting as a stent for the skin graft, was pressed into its proper position. As the stent was of clear acrylic material it could be seen that the entire denuded area was covered with the graft. (Fig. 6.) The lower denture was placed in position and elastic traction was then secured beneath the chin to stabilize the dentures firmly in centric occlusion.

The following day the patient was out of bed and comfortable. Temperature, pulse and respiration were normal. On December 10, 1952, the dentures and sutures were removed and the entire recipient area was found to be epithelialized with the split-thickness skin graft. (Fig. 7.) The patient had experienced no pain. Complete recovery was observed by December 31, 1952. (Fig. 8.)

The patient was referred to a cancer detection service and there has been no evidence of metastasis to date.

Pathologic report (No. 42384) revealed the following: Lesion of the palate: There was a section of mucous membrane measuring 6 by 5 by 2 cm., in the central portion of which was a hard, nodular, ulcerating mass measuring approximately 1.5 cm. in diameter. (Fig. 9.)

The mucous membrane overlying the tumor mass was ulcerated. There was a very severe inflammatory reaction throughout the tissue consisting of polymorphonuclears, lymphocytes and plasma cells. Sections through the tumor showed it to be a well circumscribed but not encapsulated mass. There were capillary spaces surrounded by large clear cells with small vesicular nuclei. The cells tended to form mosaic cell nests about the blood spaces.

The diagnosis was hemangioendothelioma.

COMMENTS

A case of hemangioendothelioma has been presented with surgical intervention and effective immediate skin graft.

This case is typical of this type of tumor since it possesses many of the characteristics usually found in the hemangioendotheliomas. The histopathologic section shows the proliferation of the type of cells found lining blood vessels. This cell is of mesodermal origin,[5] and therefore this tumor belongs in the category of sarcoma.

A review of the previous sections of tumors removed from this patient showed that these other tumors could also be called hemangioendothelioma. It was believed by the pathologists that many of the characteristic cells were definitely present. This would then fit into the clinical picture associated with these vascular tumors, in that they are multifocal and recurrent in nature, as described by Stout.[7]

Trauma as a possible etiologic factor was advanced by Busman,[5] Sweitzer and Winer.[6] In this case this possibility exists since the site of the lesion was covered by an ill-fitting denture.

Wide thorough excision as advocated by Sweitzer and Winer[6] is believed to be effective in the treatment of hemangioendothelioma. In the case presented recurrence appeared after seven months when the lesion was removed only for biopsy.

Approximately a year and a half has elapsed since the surgical removal of the lesion and to date there is no sign of recurrence. The effectiveness of the skin graft was definitely shown in that complete healing occurred in approximately eighteen days, and the patient experienced no discomfort during this time.

Immediate skin grafting is a valuable adjunct to the surgeon. By covering large denuded areas anywhere in the body including the oral cavity, the healing time can be shortened considerably. The viability of denuded bone is preserved and infection is prevented. Certainly this adds to the comfort of the patient. In soft tissue early coverage minimizes cicatrization and deformity. Skin grafting should always be considered when a large area is surgically denuded.

SUMMARY

A rare case of hemangioendothelioma of the palate is reported.

The method of treatment was wide excision of the lesion with immediate split-thickness skin graft.

The healing was complete in eighteen days.

Approximately a year and a half postoperatively there has been no local or general evidence of metastasis.

Acknowledgment: The authors wish to acknowledge the fine work done by the Department of Pathology of New York City Hospital, under the direction of Dr. James Lisa, in the histopathologic diagnoses presented in this article.

REFERENCES

1. Mallory, F. B. The Principles of Pathologic Histology, p. 319. Philadelphia, 1914. W. B. Saunders Co.
2. Drucker, V. Hemangioendothelioma—a rare malignant tumor. *Radiology*, 49: 231–237, 1947.
3. Cheyne, V. D. and Silberstein, H. E. Hemangioendothelioma. *Am. J. Orthodontics*, 28: 703–721, 1942.
4. Maximov, A. A. and Bloom, W. A Textbook of Histology, 3rd. ed., p. 31. Philadelphia, 1938. W. B. Saunders Co.
5. Busman, G. J. Malignant endothelioma with cutaneous involvement. *Arch. Dermat. & Syph.*, 6: 680, 1922.
6. Sweitzer, S. E. and Winer, L. H. Hemangioendothelioma. *Arch. Dermat. & Syph.*, 34: 997, 1936.
7. Stout, A. P. Hemangioendothelioma; tumor of blood vessels featuring vascular endothelial cells. *Ann. Surg.*, 118: 445–464, 1943.

Intussusception Due to Invaginated Meckel's Diverticulum after Previous Appendectomy

M. C. TADDEO, M.D. AND H. H. JANES, M.D., *New York, New York*

From the First Surgical Division, Fordham Hospital, Bronx, New York.

MECKEL'S diverticulum and intussusception occurring individually are relatively common. However, together they are uncommon. The earliest case of intussusception due to invaginated Meckel's diverticulum is the specimen placed in St. Bartholomew's Hospital Anatomical Museum in 1846. Harkins, in 1933, could find only 160 cases in the literature in which Meckel's diverticulum was a direct or indirect cause of intussusception.[6]

In cases diagnosed as acute appendicitis, in which the appendiceal pathology is not concomitant with the severity of clinical symptoms, a thorough investigation of the ileum should be made prior to removing the appendix. It is not satisfactory to investigate the terminal 1 to 2 feet of ileum, but rather the distal 3 to 4 feet. The patient in the case presented herein had had an appendectomy performed two years prior to admission, in which the pathologic diagnosis was chronic lymphoid appendix and only 1½-feet of terminal ileum had been examined. In all probability, had the terminal 3 to 4 feet of ileum been explored, a diagnosis of Meckel's diverticulitis or other affectation would have been made and diverticulectomy performed at that time, preventing the subsequent occurrence of intussusception. In addition, this introduces another etiologic factor in the pathogenesis or mechanism of production of Meckel's invagination, namely postoperative appendiceal adhesions as a predisposing cause.

In our case the invaginated Meckel's diverticulum was the lead point of the intussusception and may have been started by postoperative appendiceal adhesions or by the presence of a disturbance within the diverticulum itself which contained heterotopic gastric mucosa. Martin states in cases of Meckel's intussusception in which the diverticulum contained heterotopic gastric tissue and is the starting point of the intussusception adds to the rarity of this condition.[17]

CASE REPORT

S. E., an eleven year old white boy, was admitted to the hospital on March 6, 1953, with chief complaints of pain in the right lower quadrant, nausea and vomiting of two days' duration. His pains were rhythmic and colicky in character. Previous to admission the patient had vomited yellowish green material on several occasions.

Past history revealed he had had an appendectomy on April 25, 1951, in which the pathologic report was chronic lymphoid appendix. At operation there was no free fluid in the peritoneal cavity nor was there any remarkable disorder of the appendix. The terminal ileum was explored for 1½ feet and was normal. The patient had an uneventful recovery.

Physical examination disclosed that the boy was acutely ill, complaining of abdominal pain and vomiting with moderate abdominal distention. Abdominal examination revealed tenderness in both lower quadrants, no rigidity, no palpable masses, no rebound tenderness, and normal liver and spleen. Rectal examination revealed an empty ampulla, tenderness to the right and no palpable mass. All other systems were normal.

Laboratory data were as follows: Scout film of the abdomen revealed distention of the small intestine with fluid levels indicating obstruction. Leukocyte count was 11,900 with 86 per cent segmented cells, 10 per cent lymphocytes and 4 per cent monocytes. Hemoglobin was 12.1 gm. Diagnosis on admission was small bowel obstruction secondary to postoperative adhesions.

Exploratory laparotomy was performed on the day of admission. A right lower paramedian skin incision was made. Upon opening the

peritoneum, a moderate amount of straw-colored fluid was noted. This was suctioned off and a culture was made. Loops of ileum, distended with fluid, were noted. Exploration revealed an adhesive band extending from the omentum down to the right inguinal region in the area of the old McBurney scar, partially compressing the ileum. The adhesion was severed between clamps and ligated. No appendix was found. The cecum was bound down by numerous adhesions but was not distended. The small bowel was systematically explored starting at the ligament of Treitz. Approximately 3 feet from the ileocecal junction an ileo-ileal intussusception was found, in which the proximal ileum was invaginated within the terminal ileum for approximately 1 foot. By gentle taxis the bowel was milked out and freed of its intussusception without difficulty, thus collapsing the distended ileum. Three and a half feet from the ileocaecal valve a dimpling was noted on the antimesenteric border of the ileum, and upon gentle compression edematous Meckel's diverticulum, about 2 inches long, was expressed. The base of Meckel's diverticulum was wide, measuring about ¾ inch in diameter. There was no discoloration of the bowel. The diverticulum was excised at its base and the opening closed transversely. The wound was closed in layers.

Pathologically, the specimen revealed Meckel's diverticulum containing heterotopic gastric mucosa.

The patient's postoperative course was uneventful and he was discharged on the seventh postoperative day.

COMMENTS

Embryology and Anatomy. In early fetal life the mid-gut has a wide communication with the yolk sac. As the abdominal walls approximate one another, the vitello-intestinal duct becomes narrower and lies within the umbilical cord. Under normal conditions the intestine finally is set free from all connection with the yolk sac and retires within the abdominal cavity, with obliteration of the vitello-intestinal duct. The vitello-intestinal duct may fail to undergo complete obliteration and may be found with its intestinal end attached to some portion of the ileum near the ileocecal valve and its distal end free. This abnormality is known as Meckel's diverticulum. Its length varies from ½ inch to 2 or 3 inches, and in infants is usually located 18 inches proximal to the ileocaecal valve. It must be borne in mind that the location of the diverticulum varies with the age of the patient. As the child grows older with increased lengthening of his intestine, Meckel's diverticulum will be found at greater distances from the ileocaecal valve proportionately. Thus in adolescents and adults the diverticulum may be 3½ to 4 feet proximal to the ileocecal junction. Hence, at operation, when exploring the terminal ileum for Meckel's diverticulum, the surgeon must examine at least 4 feet of ileum before he decides the diverticulum is not present. Several cases have been presented in the literature in which the diverticulum was located 4 feet proximal to the ileocaecal valve.[11]

Incidence. Meckel's diverticulum is found in 2 per cent of normal persons. The incidence of Meckel's diverticulum in acute intussusception is not high. Of 2,414 cases collected by Harkins only 2.5 per cent were associated with Meckel's diverticulum.[6]

The relationship of intussusception due to Meckel's diverticulum and other diseases of Meckel's diverticulum was as follows: Porter found 20 cases of intussusception in a series of 184 affections of Meckel's diverticulum; Forgue and Riche found 34 intussusceptions in 287 cases of obstruction due to the organ; Drummond found 7 of 22 and Wellington, 59 of 326. Thus 17 per cent of Meckel's diverticula produced intussusception.

Age and Sex Incidence. Meckel's intussusception occurs in older age groups as compared to the acute infantile intussusceptions. The average age is 13.1 years, 60 per cent of the cases occurring between 0 to 10 years of age and 24 per cent between 11 to 20 years of age. Since the preponderance of Meckel's diverticula and intussusception occurring separately is in males, it is not surprising to find that the frequency of Meckel's diverticulum with intussusception occurs more commonly in males. In Harkins' series of 105 cases, 79 per cent occurred in males.

Pathogenesis. Intussusception associated with Meckel's diverticulum almost always finds the diverticulum as the lead point of the intussusception. The question arises as to whether the diverticulum invaginates primarily or secondarily. The bulk of evidence favors the view that the invagination of the diverticulum is primary and more likely to occur when there

is an inflammatory condition or other pathologic disorder in progress within the diverticulum.[17] Predisposing causes, such as a diseased appendix or postoperative adhesions causing partial obstruction of the terminal ileum, may start the diverticulum to invaginate. Once the diverticulum has invaginated, it will act in much the same way as a pedunculated polyp or other neoplasm which gets passed down the gut by peristalsis, acts as the lead point and causes the intussusception.[15] In our case both etiologic factors were present. A large postoperative adhesive band was found compressing the terminal ileum and inflammed, congested heterotopic gastric mucosa was found within Meckel's diverticulum.

Gray and Kernohan[24] reported a case of Meckel's intussusception with heterotopic gastric mucosa in which adenocarcinoma had arisen from the gastric mucosa of the diverticulum and acted as the lead point of the intussusception. Other neoplasms such as adenomas, carcinoids and sarcomas may occur in Meckel's diverticulum, causing the diverticulum to invaginate and start an intussusception.[24]

Clinically, Meckel's diverticulum with intussusception runs a subacute course as compared to the acute picture presented in other types of intussusception. In many cases symptoms were of long duration and it was difficult to tell exactly when the present illness had begun. Corner states that "as the origin of the invagination is lateral, the ring where the bowel is infolded is very oblique, and consequently the intestinal lumen is not completely occluded, and the case may be clinically subacute. "Meckel's intussusception may simulate appendiceal abscess although the rapidity of development, rather low temperature and pulse rate are arguments against the diagnosis of appendiceal abscess.[3] Often a large mass is palpable in the right iliac fossa suggesting the diagnosis of appendiceal abscess. All intussusceptions produce some melena but in general, Meckel's intussusception does not produce as much. The explanation suggested is that the diverticulum becomes swollen and edematous and obstructs the intestine, thus preventing marked melena. In addition, the apex of the intussusception never reaches the rectum and hardly ever the hepatic flexure. However, other intussusceptions may reach the rectum.

In differential diagnosis the conditions most frequently confused with Meckel's intussusception are: (1) appendicitis, (2) intussusception without Meckel's diverticulum and (3) other affections of Meckel's diverticulum.[6] The pain in Meckel's intussusception is apt to be colicky, there may or may not be blood in the stool and the rigidity or tenderness of appendicitis may not be present. The only differentiation from affections of Meckel's diverticulum is that the characteristics of an intussusception are not present. The differential diagnosis is very difficult since both present signs of intestinal obstruction.

Differentiation from other forms of intussusception is based upon the following: occurs in older individuals, signs of intussusception are atypical, pain and vomiting are more common, definite melena and a palpable rectal mass are rarer. A mass may possibly be felt in the right lower quadrant, while in ordinary intussusception a mass is more commonly felt on the left side. A history of previous attacks and the chronic course of the condition speaks for intussusception due to a Meckel's diverticulum.

Treatment. Surgical intervention should be carried out as soon as the diagnosis is made. The types of operations that may be employed are as follows: (1) simple reduction, (2) additional resection of diverticulum, (3) bowel resection, (4) miscellaneous procedures such as colostomy, Mikulicz colostomy and obliteration of the lumen of the diverticulum.

The choice of operation is reduction and excision of the diverticulum; and if bowel resection is necessary, it is less dangerous than in ordinary intussusceptions because the patients are older. Much discussion has occurred as to whether the diverticulum should be resected. Bidwell's experience is in favor of removing the diverticulum, and Harkins states "that the only recurrence in his series was one of the cases in which he did not resect the diverticulum." After excising the diverticulum the incision in the ileum should be repaired transversely. Purse-string suturing of the incision is to be condemned.

SUMMARY

1. An eleven year old boy with a preoperative diagnosis of intestinal obstruction secondary to postoperative adhesions was operated upon and found to have a Meckel's diverticulum with intussusception. Reduction of the intussusception and excision of the diverticulum resulted in a cure. Appendectomy

had been performed two years prior to this admission and pathologic diagnosis was chronic lymphoid appendix. Inadequate exploration of the terminal ileum resulted in a failure to discover the presence of a Meckel's diverticulum. Case report and a review of the literature is presented.

2. In cases diagnosed as acute appendicitis, in which the appendiceal pathology is not concomitant with the severity of clinical symptoms, a thorough investigation of the ileum should be made prior to removing the appendix. It is not satisfactory to investigate the terminal 1 to 2 feet of ileum but rather the distal 3½ to 4 feet should be explored.

3. Meckel's intussusception occurs in older age groups as compared to the acute infantile intussusceptions. The average age is 13.1 years, with a preponderance in males (79 per cent).

4. Clinically Meckel's diverticulum with intussusception runs a subacute course as compared to the acute picture presented in other intussusceptions.

5. Conditions most frequently confused with Meckel's intussusception are: (1) appendicitis, (2) intussusception without Meckel's diverticulum and (3) other affections of Meckel's diverticulum.

6. The choice of operation is reduction of the intussusception and excision of the diverticulum. If bowel resection is necessary, it is less dangerous because the patients are in older age groups as compared to the acute intussusceptions of infancy and early childhood.

REFERENCES

1. Roentgen diagnosis of invagination of small intestine; study of its causes. *Acta radiol.*, 13: 362, 1932.
2. Bettazzi, G. Intussusception caused by Meckel's diverticulum, clinical report of case. *Boll. e mem. Soc. piemontese chir.*, 2: 925–946, 1932.
3. Clark, H. S. Intussusception simulating appendiceal abscess. *South. Med. & Surg.*, 95: 270, 1933.
4. Schaaf, G. Ileocaecal invagination after appendectomy, case. *Deutsche Ztschr. f. Chir.*, 241: 121, 1933.
5. Raiser, E. Invagination of small intestine caused by Meckel's diverticulum. *Röntgenpraxis*, 7: 90–94, 1935.
6. Harkins, H. N. Intussusception due to invaginated Meckel's diverticulum; report of 2 cases with study of 160 cases collected from literature. *Ann. Surg.*, 98: 1070–1095, 1935.
7. Duncan, G. Intussusception due to invagination of Meckel's diverticulum. *Lancet*, 2: 1174, 1935.
8. Ladd, W. E. and Gross, R. E. Intussusception in infancy and childhood; 372 cases. *Arch. Surg.*, 29: 365–384, 1934.
9. Korzun, P. I. Invagination of Meckel's diverticulum; case. *Sovet. khir.*, 8: 76–78, 1935.
10. Klingenstein, P. Enteric intussusception due to invagination of Meckel's diverticulum. *J. Mt. Sinai Hosp.*, 3: 1–6, 1936.
11. Johns, J. Low ileum intussusception caused by Meckel's diverticulum; case. *J. Michigan M. Soc.*, 37: 1083, 1938.
12. Pool, R. M. and Porter, C. H. Intussusception due to inverted Meckel's diverticulum. *Am. J. Surg.*, 80: 368–370, 1950.
13. Hogg, B. M., Donovan, E. J. Acute intussusception in infants and children. *Ann. Surg.*, 124: 262–267, 1946.
14. Grigorescu, I. I. Chronic ileo-iliac invagination due to Meckel's diverticulum. *Rev. stiint med.*, 29: 913, 1938.
15. Paul, M. Enteric intussception due to invagination of Meckel's diverticulum. *Brit. M. J.*, 1: 504, 1939.
16. Couvelaire, R. and Bret, J. Mechanism of production of acute invagination in adolescents. *Arch. d. mal. de l'app. digestif.*, 29: 97–100, 1939.
17. Martin, W. S. Meckel's diverticulum containing gastric tissue as cause of intussusception; résumé of literature and report of case. *J. Michigan M. Soc.*, 38: 590, 1939.
18. D'Agata, G. Two cases of ileocaecal invagination in children; pathogenesis. *Arch. ital. chir.*, 51: 496, 1938.
19. Hanelin, H. A. Meckel's diverticulum, invagination. *J. Michigan M. Soc.*, 39: 786, 1940.
20. Sprague, J. R. and Srigley, R. S. Intussusception due to Meckel's diverticulum; 4 cases. *Ohio State M. J.*, 37: 843–845, 1941.
21. Clark, C. W. Irreducible double intussusception due to Meckel's diverticulum complicated by volvulus. *Brit. J. Surg.*, 31: 301–303, 1944.
22. Hindmarsh, F. D. Gangrenous enteric intussusception in adolescence. *Brit. M. J.*, 2: 122, 1946.
23. Holm, C. Intussusception as complication after appendectomy; case. *Acta chir. Scandinav.*, 96: 308–312, 1948.
24. Gray, H. K. and Kernohan, J. W. Meckel's diverticulum. *J. A. M. A.*, 108: 1480, 1937.

Temporal Artery Aneurysm

WILLIAM L. MARTIN, M.D., AND WILLIAM C. SHOEMAKER, M.D.,
Philadelphia, Pennsylvania

From the Department of Surgery, Hahnemann Medical College and Hospital, Philadelphia, Pa.

ANEURYSMS of the temporal artery are uncommon; when they occur they are usually traumatic in origin and often arise following a laceration or an open wound. The following case report is unusual in that no history of trauma was elicited after careful interrogation and no external evidence of trauma was apparent on the skin or surrounding tissues.

CASE REPORT

H. F. W. (Case No. 94959), a sixty year old white man was admitted with the complaint of a small mass in the right temporal area (Fig. 1) which had slowly increased in size since its onset five years previously. There was no pain or other symptoms and no history of trauma. The patient felt a pulsating sensation in the region of the mass. There was no inflammation or drainage.

Family history revealed that the father of the patient died of arteriosclerosis at seventy-two, and the mother of hypertension and valvular heart disease at forty-nine.

Past medical history of the patient included hypertension (over 200 mm. systolic) for over two years and repair of a perforated duodenal ulcer at forty-eight years of age with secondary repair of an incisional hernia at fifty-eight years.

Systemic review disclosed some exertional dyspnea and precordial pain radiating to left shoulder and elbow. There were no other cardiorespiratory symptoms.

Physical examination revealed a sixty year old white man who was somewhat overweight (174 pounds); temperature was 98°F., pulse 82, respiration 20, blood pressure 190/100. Pertinent findings included a 1 cm. pulsating mass in the right temporal region. The mass could be obliterated with digital pressure over it and the collapsed state could be maintained as long as pressure was held over the vessel immediately above and below it. An accentuated aortic second sound was heard and occasional premature beats were observed.

X-ray examination of the skull was essentially negative. Blood counts, urinalysis, routine blood chemistry studies and serology were negative or within normal limits.

On November 20, 1953, an operation was performed by the senior author (W. L. M.). The afferent and efferent arterial segments were ligated three times through a small incision with silk and severed. The aneurysm was separated from the surrounding tissue by means of sharp and blunt dissection with relative ease and little or no bleeding. The aneurysm together with short segments of the normal artery was then removed *in toto* and the wound was closed in layers with silk sutures. (Fig. 2.)

The skin sutures were removed on the second and third postoperative days and wound healing was considered satisfactory. The patient was discharged on the second postoperative day.

Pathologic examination of the specimen revealed an arteriosclerotic aneurysm with dilatation and thickening of the walls, particularly marked in the media. (Fig. 3.) There was minimal infiltration of the vessel wall with polymorphonuclear leukocytes and lymphocytes.

COMMENTS

Winslow and Edwards,[1] in an exhaustive review of the literature, found ninety-three cases of temporal artery aneurysm. Of these, seventy-nine, or 85 per cent, were considered to be traumatic in origin. Of these seventy-nine cases, forty-one were associated with an open wound, while thirty-three were associated with contusions only. Nine cases were thought to have arisen spontaneously. The origins in the remaining five cases were either not discussed or unknown. Since Winslow's extensive paper in 1934 we have found only one other case,

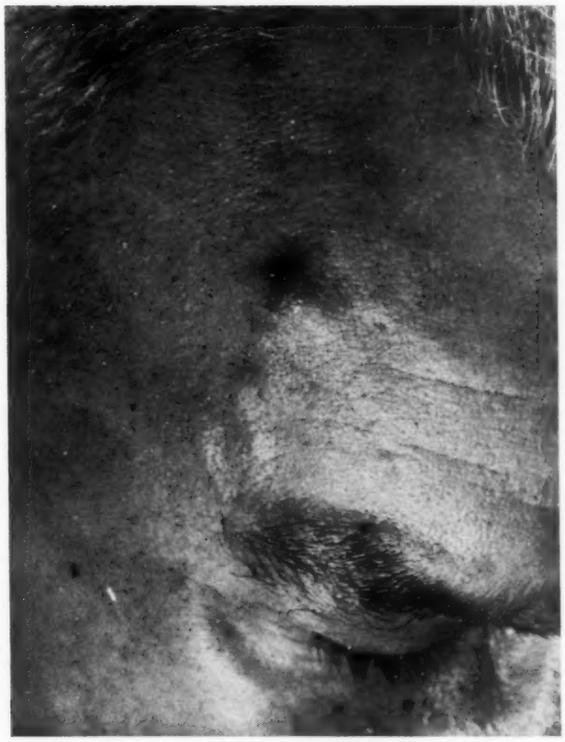


FIG. 1. Surface appearance of aneurysm of right temporal artery.

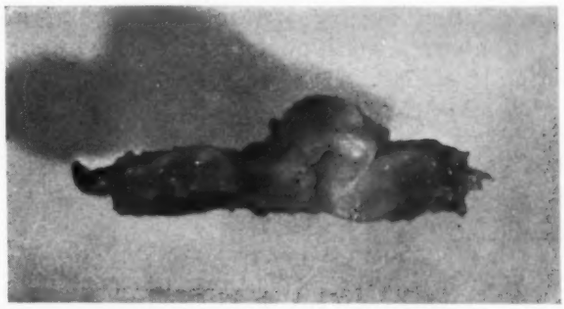


FIG. 2. Aneurysm with proximal and distal artery dissected out.

that of a traumatic temporal artery aneurysm reported by Tippett.[2]

This case assumes significance not only because of its rarity but also because of a possible relationship to intracranial aneurysms. The mechanics involved in the development of these so-called congenital aneurysms was first investigated by Forbus.[3] He demonstrated defects in otherwise normal cerebral arteries in the muscular coat at the angles made by their bifurcations. Turnbull[4] believed that the defect in the media was much more common in the cerebral arteries than in other arteries of the muscular type. Forbus[3] also observed degeneration of the internal elastic membrane in the areas corresponding to the medial defects.

Subarachnoid hemorrhage has been attributed, in the main, to this type of phenomenon. However, in a significant percentage of cases arteriography or exploratory craniotomy or both fail to reveal congenital aneurysms after thorough and painstaking search. The possibility exists that an aneurysm such as the one described herein may arise spontaneously in the smaller branches of the arterial supply of the brain. Such an aneurysm would be more prone to arise in the brain where the supporting stroma is softer, less dense and more easily compressed. The initiating factors in the production of such a condition theoretically may be arteriosclerosis, trauma or cryptogenic. Tiny intracranial hemorrhages produced from aneurysmal defects of the lesser vascular radicals would be difficult to demonstrate, and the condition at postmortem examination might be almost entirely obscured by the

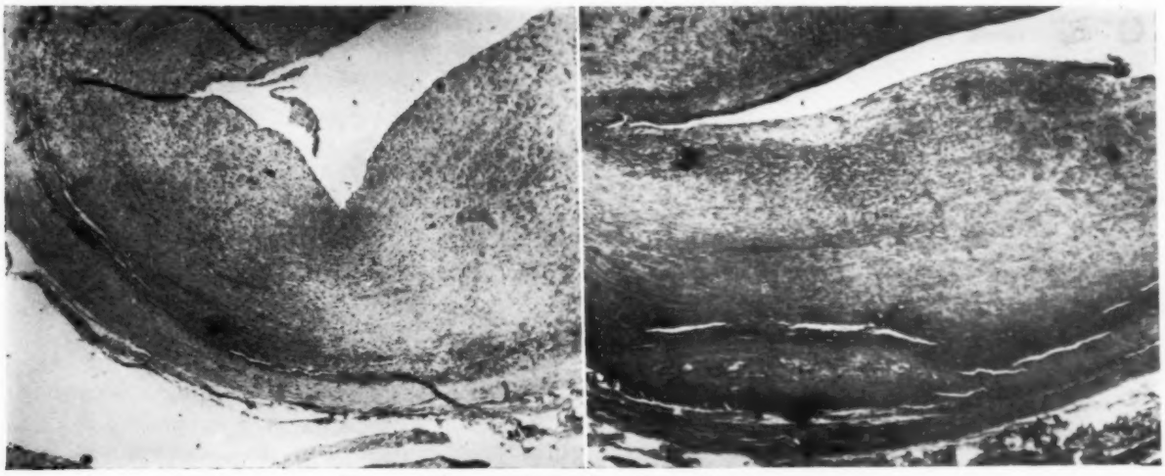


FIG. 3. Microscopic sections through aneurysm.

surrounding hemorrhage to such an extent that only time-consuming serial sections would bring it to light.

SUMMARY

1. A case of temporal artery aneurysm thought to be due to arteriosclerosis is presented.

2. A possible relationship of this type of vascular defect to intracranial hemorrhage is postulated.

REFERENCES

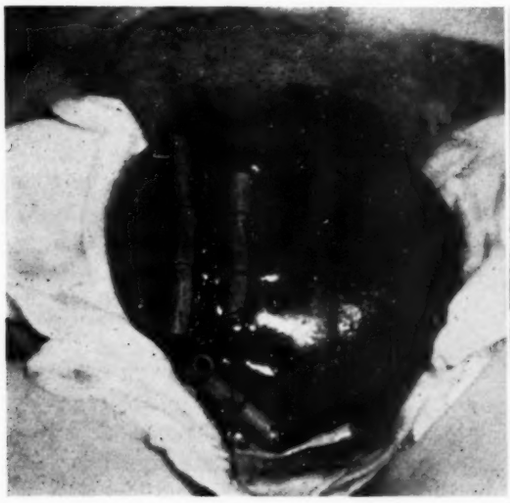
1. Winslow, N. and Edwards, M. Aneurysm of the temporal artery. *Bull. School Med. Univ. Maryland*, 19: 57–72, 1934.
2. Tippett, G. Two cases of traumatic aneurysm. *Brit. M. J.*, 2: 711–712, 1932.
3. Forbus, W. D. On the origin of miliary aneurysms of the superficial cerebral arteries. *Bull. Johns Hopkins Hosp.*, 47: 239–284, 1930.
4. Turnbull, H. M. Alterations in arterial structure and their relation to syphilis. *Quart. J. Med.*, 8: 201–254, 1914–15.

Working with vaginal secretions in 1928 Papanicolaou noted that he could distinguish cancer cells from normal ones by their irregularity in size and shape, by their large hyperchromatic nuclei with large nucleoli, and their altered nuclear, cytoplasmic relationships. Later, investigators began to apply this same principle to examination of other body fluids and secretions, as from the stomach, the prostrate gland, etc., in the hope of making an earlier diagnosis of any possible malignancy. Similarly, the sputum, bronchial secretions and bronchial washings have been subjected to cytologic examination often with very satisfactory results. Bronchial washings are exceptionally valuable. About 5 cc. of saline solution are injected into the suspicious bronchus during bronchoscopic examination and then are recovered and examined, usually by the smear method, fixing the freshly made smear (on glass slide) into a solution that is half ether and half 95 per cent alcohol. Some authors use pieces of gelfoam to obtain their material, then place it in a paraffin block and dissect it as in histologically examining any other piece of tissue. In either case excellent results are possible if one is thoroughly experienced with cytologic work. (*Richard A. Leonardo, M.D.*)

Spontaneous Rupture of a Hydrocele Testis

MONROE WOLF, M.D. AND F. R. GOMILA, JR., M.D., *New Orleans, Louisiana*

HERBUT,[1] in describing the complications of hydrocele testis, makes no mention of spontaneous rupture. However in describing hematocele testis he quotes Neligan[2] erroneously, stating that hematocele testis may come on spontaneously. A thorough search of the literature has failed to reveal a case similar to the one presented herewith.



1

2

FIG. 1. Marked ecchymosis twelve hours postoperatively.

FIG. 2. Marked regression sixty hours postoperatively, with the Penrose drain removed.

CASE REPORT

L. D., a sixty-two year old white automobile mechanic, consulted Dr. G., who asked me to see the patient because of marked ecchymosis of the scrotum, penis, prepubic area and both thighs. There was a history of hypertension of several years' duration and chronic hydrocele testis of three years' duration. The hydrocele had been tapped at sixteen to eighteen-week intervals, the last time approximately twelve weeks previously.

Examination on November 30, 1953, revealed a robust man of the apparent age stated previously with a facial expression of slight general discomfort. The history, as stated by the patient, was that on the previous afternoon he had had a sudden attack of pain in his right scrotum with no history of trauma. After going home from work he had noted that the scrotum was more swollen than it had been and had turned a bluish black color, the discoloration extending into the penis. There was an increase in discomfort.

The external genitalia presented a markedly enlarged right scrotum, highly ecchymotic, the ecchymosis extending into the subcutaneous tissues of the penis, prepubic area and the anterior medial aspects of both thighs. The prepuce was edematous and retracted (paraphimotic) about the corona. The scrotum would not transilluminate light.

Physical examination revealed the following: Blood pressure 200/120; heart rate irregular, extrasystole, no murmurs, ro rubs; lungs negative; abdomen and external genitalia revealed ecchymosis of the lower abdomen in the prepubic area, marked swelling and ecchymosis of the right scrotum, paraphimosis of the prepuce; mild ecchymosis of the upper aspects of both thighs.

FIG. 3. Six days postoperatively, the day of discharge from the hospital. The skin is practically normal in color.

The laboratory reports were essentially negative.

When the patient was seen at 7:30 P.M., about two hours after hospital admission, the scrotum had increased in size about 50 per cent, the ecchymosis was considerably more marked and the patient was suffering with greater discomfort. It was decided to proceed with surgery without further delay.

An incision, 3 inches in length, was made through the skin and the integument of the scrotum (right), including the markedly thickened hydrocele sac wall. Approximately 200 cc. of organized blood clots were evacuated from within the tunica vaginalis. Upon everting the incised scrotal edges, an irregular tear in the sac wall was noted medial to the upper margin of the wound. There was a venous ooze from the medial edge of this torn surface. The subcutaneous tissue and all fascial planes were markedly infiltrated with extravasated blood. The hydrocele sac was partially separated and the redundant, thickened sac wall excised. The lower two-thirds of the sac which remained were sutured behind the testis with interrupted No. 00 plain catgut sutures.[2] A counter incision was made in the most dependent portion of the scrotum, through which a small Penrose drain was applied. The skin was closed with through and through vertical mattress sutures of black silk tied over small rubber tubing. Pentothal®, nitrous oxide anesthesia was used. The patient returned to the ward practically awake, in very good condition. Postoperative reaction of the tissues was satisfactory. (Figs. 1–3.)

On January 22, 1954, the patient visited the office. He had been working regularly since December 10, 1953, with no discomfort. The scrotum was normal in size, color, shape and consistency.

SUMMARY

A case of spontaneous rupture of hydrocele testis with tearing of a blood vessel creating a hematocele in the hydrocele sac concomitantly with paraphymosis and extravasation of blood into the scrotal wall, penis, lower abdomen and thighs is reported.

The necessity for early exploration and arrest of active bleeding is mentioned.

REFERENCES

1. HERBUT, P. A. *Urological Pathology*, 2: 1181, 1952.
2. NELIGAN, G. E. Traumatic orchitis and hematocele. *Practitioner*, 136: 496, 1936.

Acute Appendicitis from Gunshot Trauma

JULIEN M. GOODMAN, M.D., *Nelsonville, Ohio*

TRAUMA is admittedly a rare cause of acute appendicitis. However, the causal relationship between trauma and appendicitis merits special consideration not only because of the uncertainty as expressed in the literature, as to whether injury actually can produce acute appendicitis, but also because of the possible medico-legal implications if such an etiology can be proved. A case apparently qualifying as true traumatic appendicitis has recently been observed and is the basis of this report.

A review of the literature on the subject reveals a diversity of opinion. A study of the problem has evidently been given impetus by the claims for disability filed with industrial commissions of various states for acute appendicitis allegedly caused by injury.

Bate[1] doubted that trauma could be considered an etiologic factor in appendicitis, after reading in the literature of such inciting "traumatic" causes as walking, dancing, running, stooping, lifting and falling; in fact the inclusion of most of the activities that make up our daily lives. Pease[8] began his investigation believing that traumatic appendicitis was of doubtful occurrence, but ultimately concluded that it was a definite clinical entity and deserving of recognition by both physicians and courts. After an extensive review of cases, Fowler[6] expressed his belief that proof of trauma as a cause of appendicitis rested upon three premises: (1) History of no previous attacks. (2) The causative traumatism must be capable of reacting upon and affecting the appendix; the injuring object must be large; the force must be direct, blunt, violent and of limited duration. (3) The effects of the trauma must be experienced immediately, must merge into symptoms of acute appendicitis, must be promptly reported, must be disabling and must require medical attention and surgical operation at once.

The evidence makes it difficult to justify a categorical repudiation of a possible relationship between abdominal injury and appendicitis. In cases of direct trauma to the lower right abdomen it appeared undeniable to Courtney[5] that external or internal injury of the appendix might occur. However, Connell[4] believed that any injury severe enough to cause appendicitis by interference with the blood supply of the appendix would cause considerable damage to the cecum and surrounding intestine as well as the abdominal wall. This conclusion was concurred in by Rhodes and Birnbaum[9] who approved a diagnosis of traumatic appendicitis only if there were free blood in the peritoneal cavity or histologic evidence of trauma.

In papers dealing with this subject it is notable that authors seem to be very wary in the selection of words that concede the plausibility of a connection between appendicitis and trauma yet sidestep an unequivocal acceptance of such a relationship. For instance, Black[2] wrote: "Abdominal trauma as a causative or contributory factor in the development of acute appendicitis occasionally merits attention, as the symptoms of that condition have appeared very soon after receipt of the injury." After Burgess[3] reviewed a long series of cases reported in the literature, he admitted that coincidence alone would be overtaxed to explain the phenomenon. The probable existence of acute traumatic appendicitis received support by the three proven cases reported by Macht.[7] Two cases followed trauma to the right lower abdominal quadrant; the other case was that of a woman having a deep lying pelvic appendix, in whom appendicitis developed after prolonged and violent sexual intercourse. Resultant appendiceal pathologic condition in a young man, satisfying the three premises of Fowler, and similar to the cases of Macht is reported here.

CASE REPORT

A man seventeen years old, of asthenic build, with no recent illness and no history of previous right lower quadrant abdominal pain, was brought to the hospital fifteen minutes after he had been accidentally shot by a .22 calibre rifle. The wound of entrance was on the

anterior abdominal wall about 2 cm. below McBurney's point, and the wound of exit was in the right lumbar region. There was pronounced abdominal rigidity but no evidence of peripheral vascular collapse. Immediate exploratory laparotomy was done to determine the extent of internal injury.

The abdomen was opened by a right pararectus incision. In the abdominal cavity there was free blood that was suctioned off during inspection of the entire gastrointestinal tract. The only damage found was a serosal tear of the medial aspect of the cecum and a perforation of the ileocecal fold, resulting in a denuded area. The appendix itself was not injured and the mesoappendix was not torn. The bleeding was from small terminal branches of the ileocolic vessels which were easily located and ligated. The appendix was removed routinely; the serosa was reapproximated over the cecum and the abdomen was closed without drainage.

The patient received parenteral nutrition for twenty-four hours, tetanus-gas gangrene toxin-antitoxin prophylactically, and chlortetracycline 250 mg. every six hours. Under this regimen he made a smooth, uneventful recovery, his temperature returning to normal on the second postoperative day and remaining there throughout the remainder of the hospital stay. He was discharged on the ninth postoperative day in good condition.

Pathologic report was as follows. Grossly, the specimen consisted of an appendix 10 cm. long, 7 mm. in diameter, slightly injected and otherwise of normal appearance. Microscopically, the lumen contained some blood clot and fecal material. The mucosa was intact. Lymphoid tissue was of average amount. A moderate amount of purulent exudate was found in the wall. Diagnosis was early acute appendicitis.

COMMENT

The sequence of events in the case reported herein supports the diagnosis of indirect trauma as a cause of the acute appendicitis. Although the injury was a perforating gunshot wound of the abdomen, the effect on the appendix was entirely indirect as proved at laparotomy when no gross injury to the appendix or its immediate blood supply could be demonstrated. The inflammatory changes in the appendix were consistent with an onset one hour and fifty minutes previously: the time the gunshot wound was incurred. Although it is theoretically possible that acute appendicitis was developing at the time the patient was shot, no recollection of abdominal pain preceding the injury could be elicited. It would therefore seem more logical to attribute the inflammatory changes to the trauma, and acknowledge this as the correct explanation.

SUMMARY

1. The difficulty of establishing a causal relationship between trauma and acute appendicitis is discussed and the pertinent literature is briefly reviewed.

2. A case of early acute appendicitis resulting from indirect trauma (gunshot wound injuring the cecum but not the appendix) is presented.

REFERENCES

1. Bate, J. T. Appendicitis induced by trauma. *Am. J. Surg.*, 48: 437–439, 1940.
2. Black, W. R. The role of abdominal trauma in acute appendicitis. *Brit. M. J.*, 2: 424–425, 1948.
3. Burgess, C. M. Traumatic appendicitis. *J. A. M. A.*, 111: 699–700, 1938.
4. Connell, J. E. A. Trauma and appendicitis. *Surgery*, 7: 47–60, 1940.
5. Courtney, J. E. Traumatic appendicitis. *Nebraska State M. J.*, 28: 379–380, 1943.
6. Fowler, R. H. Trauma and appendicitis. *J. A. M. A.*, 111: 466–467, 1938.
7. Macht, S. H. Traumatic appendicitis. *Virginia M. Monthly*, 75: 122–123, 1948.
8. Pease, G. N. Traumatic appendicitis. *Journal Lancet*, 59: 539–541, 1939.
9. Rhodes, G. K. and Birnbaum, W. D. Traumatic appendicitis. *California & Western Med.*, 35: 162–165, 1940.

Leiomyosarcoma of the Rectum

LT. COL. RALPH P. CAMPANALE, M.C., *Ramey Air Force Base, Puerto Rico,* AND MICHAEL J. CAVANAGH, M.D., *Brooklyn, New York*

From the 3750th U. S. Air Force Hospital, Sheppard Air Force Base, Texas.

LEIOMYOSARCOMA of the rectum is a rare tumor. In 1946 Goldman and Marbury[1] were able to find 150 cases of sarcoma of the rectum in a review of the literature, and only eight of these cases were leiomyosarcomas. Anderson, Dockerty and Buie[2] in 1950 reported ten cases of leiomyosarcoma of the rectum from the files of the Mayo Clinic for the period 1911 through 1946. A few other isolated case reports have appeared since 1950. It appears worth while, therefore, to report additional cases to the literature as they appear.

CASE REPORT

A sixty-three year old white woman was admitted to the 3750th U. S. Air Force Hospital on October 8, 1953, complaining of urinary retention. Except for chronic mild constipation of several years' duration, she had enjoyed excellent health until six months prior to admission when she noted that the constipation had become more severe and her stools had become ribbon-like. She had never noted rectal bleeding in any form or any other changes in bowel habit. Four months prior to admission she first noticed difficulty in starting the urinary stream. This became progressively worse until seven days prior to admission when retention developed and catheterization became necessary. During the previous three months she had become aware of a progressive increase in the size of her abdomen. Over the past two years she had gained 15 pounds in weight. Her appetite was good and there had been no change in her strength and vigor. The menopause had been completed fifteen years ago and there had been no episodes of vaginal bleeding or discharge since that time. Past history revealed that the patient's mother died of carcinoma of the uterus. The remainder of her past history and systemic review was non-contributory.

Physical examination revealed a well developed, well nourished, elderly white woman in no distress. Examination of the abdomen revealed slight distention of the lower abdomen with tenderness over the suprapubic region. No mass could be felt abdominally. Rectal and pelvic examination revealed an extensive rubbery ovoid mass in the retrorectal space which appeared to arise posteriorly on the left, and markedly compressed the rectum and vagina anteriorly and to the right. The mass could not be displaced and appeared to be fixed to the rectum.

Hemogram, urinalysis, stool examination, blood chemistries and liver profile studies were all within normal limits. Proctoscopic examination was performed for a distance of 18 cm. The rectum was markedly deviated anteriorly and to the right but the rectal mucosa appeared normal throughout. There was no evidence of ulceration or intraluminal tumor. X-ray examination of the chest revealed mild pulmonary emphysema. Bone survey of the pelvis and spine did not reveal any evidence of erosion or metastasis. Cystoscopic examination and retrograde urography revealed a normal genitourinary tract except for slight lateral deviation of both ureters and a posterior extrinsic pressure defect in the bladder. Electrocardiogram was within normal limits.

A preoperative diagnosis of presacral dermoid was entertained, and the patient was prepared for surgery. On October 21st, under endotracheal ether–nitrous oxide anesthesia, the abdomen was explored through a lower abdominal transverse incision. An extensive retroperitoneal tumor involving the entire true pelvis and extending well over the pelvic brim was found. The tumor was essentially ovoid, poorly encapsulated, friable and contained many areas of hemorrhage. It was easily freed from the pelvic walls and floor but was intimately adherent to the left posterolateral wall of the rectum for a distance of approximately 12 cm. The bladder was displaced anteriorly and the rectum was deviated to the right and

FIG. 1. Photomicrograph (low magnification) of lesion. (Armed Forces Institute of Pathology, Washington, D. C.)

anteriorly. Both ureters were deviated laterally and anteriorly. A frozen section of the tumor was reported as sarcoma. No evidence of metastasis in nodes, liver or extension to other abdominal viscera could be found. The tumor with the attached rectum and posterior wall of the vagina was removed in a combined abdominoperineal resection, and a permanent sigmoid colostomy was established through a stab wound in the left lower quadrant.

The patient's postoperative course was complicated by a persistent paralytic ileus which responded to intubation with a long tube, and by an abscess in the perineal incision. Following the institution of drainage, the perineal wound cleaned up rapidly and was almost completely healed when the patient was discharged on November 27, 1953.

The specimen consisted of a shredded cauliflower-like mass of pale yellow tissue assuming a somewhat lobular conformation with a consistency of fixed brain tissue. The mass measured approximately 12 cm. in diameter and weighed 250 gm. There was no demonstrable capsule. On opening the attached rectosigmoid specimen, the mucosal surface was intact and clear.

Microscopically, the tumor was composed of poorly defined fusiform cells arranged in fascicles which ran haphazardly in all directions, often with a whorled effect. The cytoplasm was indistinct and fibrillar. The nuclei were generally uniform in size and shape, their poles tending to be blunted. Mitotic activity was scattered. In some areas palisading was readily apparent. While compactly arranged for the most part, the cells in many areas were loosely arranged so as to produce a feathery pseudomyxomatous pattern. Collagen and reticulin could not be demonstrated by special staining technics. Vascularity was moderate. No invasiveness was apparent. (Fig. 1.)

Follow-up on March 30, 1954, five months after surgery, revealed that the patient was well with no evidence of a recurrence. The colostomy was functioning well.

COMMENTS

Rankin and Larson[3] in 1932 stressed that results following local extirpation were disappointing, even though leiomyosarcomas of the rectum characteristically were slow in evolution and late to metastasize. In the ten cases of leiomyosarcoma of the rectum reported by Anderson et al.[2] nine patients were known to have died of their diseases, and the tenth patient had a recurrence at the time of the report; eight of the patients were treated by local excision of the tumor with or without subsequent radium therapy, and the other two underwent immediate abdominoperineal resection with one postoperative death. These

authors described three and four local excisions because of local recurrence over a period of six to eight years in several different patients with death ultimately from abdominal sarcoidosis or metastasis. Radium therapy was believed to have no effect on the eventual outcome in this disease.

Golden and Stout[4] in 1941 recommended radical surgery for all leiomyomas of the rectum, except for the occasional pedicled leiomyoma, because of the marked tendency for recurrence to take place. Neuman[5] described a case of leiomyosarcoma of the rectum which developed from benign leiomyoma seven years after the first of two conservative enucleations.

SUMMARY

Leiomyosarcoma of the rectum is a rare but nonetheless highly dangerous malignancy. Numerous authors have repeatedly emphasized the almost invariable recurrence of this lesion after local excision, regardless of the grade of malignancy. The only hope for "cure" is radical abdominoperineal resection as the initial definitive therapy when the diagnosis has been established.

REFERENCES

1. Goldman, M. L. and Marbury, W. B. Sarcoma of the rectum. *Am. J. Surg.*, 71: 381–391, 1946.
2. Anderson, P. A., Dockerty, M. B. and Buie, L. A. Myomatous tumors of the rectum (leiomyomas and myosarcomas). *Surgery*, 28: 642–650, 1950.
3. Rankin, F. W. and Larson, L. M. Myosarcoma of the rectum. *Minnesota Med.*, 15: 833–835, 1932.
4. Golden, T. and Stout, A. P. Smooth muscle tumors of the gastrointestinal tract and retroperitoneal tissues. *Surg., Gynec. & Obst.*, 73: 784–810, 1941.
5. Neuman, Z. Leiomyosarcoma of the rectum, developing from benign leiomyoma. *Ann. Surg.*, 135: 426–430, 1952.

Omental Cyst

LT. COL. ROBERT M. HARDAWAY, III, M.C., CAPT. ROBERT N. SWARTLEY, M.C. AND CAPT. IRVING RUDMAN, M.C., *Fort Belvoir, Virginia*

From the Surgical Service, U. S. Army Hospital, Fort Belvoir, Virginia.

OMENTAL cysts are uncommon. Gross,[1] in reporting six cases, states that they originate either from a blocked lymphatic vessel or from growth of congenitally misplaced lymphatic tissue which does not communicate with the vascular system. Microscopically they are lined by a flattened layer of epithelial cells. They may be small in size and remain undetected, but frequently grow to such proportions as to fill almost the entire abdominal cavity. Symptoms are related to a slowly enlarging abdomen, usually without pain. Physical findings may be those of an enlarged soft abdomen, abdominal mass or ascites. A fluid wave can usually be elicited. Diagnosis may be difficult and is frequently not made preoperatively. Mesenteric cysts are more common and are not readily distinguished from omental cysts prior to operation. Occasionally torsion of the cyst on its pedicle may produce symptoms of an acute surgical condition of the abdomen.[2] Excision is usually not difficult and results in cure.

The following case is reported because the cyst was larger than any other which we have been able to find on record. Gross' largest case contained 1,300 cc.

CASE REPORT

A four year old white girl was admitted to the U. S. Army Hospital, Fort Belvoir, Virginia, with a chief complaint of progressive distention of the abdomen of one year's duration.

The parents stated that the child had been in good health since birth. One year prior to hospital admission they noted protrusion of the child's abdomen which persisted and increased until her appearance at this hospital. They observed no other abnormalities until two weeks prior to admission, when the patient began to complain of crampy abdominal pain (due to pressure on bowel?). There was no history of emesis, change in bowel habits, jaundice, weight loss or anemia. The child was active and had a normal mental age level.

The family history was not significant except that an aunt had active tuberculosis. However, contact of this individual with the patient was infrequent and brief.

Physical examination revealed a healthy appearing, active four year old child. The abdomen was soft but markedly distended with protrusion of the umbilicus and bulging of the flanks. There was considerable atrophy of the abdominal muscles. On palpation there was a sensation of fluctuation with a distinct fluid wave. No organs or masses could be felt. The veins of the abdominal wall were not distended. Peristalsis was normal. Physical examination otherwise showed no abnormality.

Laboratory findings were as follows: Red blood count was 4,500,000, white blood count 8,550, with a normal differential. Urinalysis was negative. Stool examination failed to reveal either ova or parasites. Liver function studies were normal. X-rays: Abdominal roentgenogram revealed the suggestion of a mass in the right abdomen and possible ascites. Upper gastrointestinal series was normal. Barium enema revealed no abnormalities. Intravenous pyelogram revealed a normal genitourinary tract bilaterally. A preoperative diagnosis of possible omental cyst was made on the basis of the evidence of a large, soft, fluid-filled abdomen with no cause for ascites.

At operation the peritoneum was entered through a right rectus muscle-splitting incision. In the entire anterior abdominal cavity there was a huge fluid-filled cyst which was free except for a cord-like attachment arising from the greater omentum. This pedicle attachment was approximately 15 cm. in length and contained many large tortuous vessels.

The cyst was delivered through the incision, and the pedicle was ligated and divided at its omental attachment. Exploration of the abdominal cavity revealed no other abnormalities. Incidental appendectomy was performed. The

abdominal wall was closed in layers with interrupted cotton sutures.

The postoperative course was uneventful. The child was discharged from the hospital eight days following operation, feeling much improved. She was in good health two years later.

Pathologic examination of the cyst revealed the following: Grossly, the specimen consisted of a cystic structure measuring 10 by 20 by 25 cm. and weighing 2.6 kg. The tissue comprising the wall of the cyst was thin, membranous tissue which readily transmitted light. There were no loculations. The surface was smooth. The small arteries and veins were prominent. On section the cyst contained about 2,500 cc. of watery-like amber fluid. The inner surface was smooth. (Fig. 1.) Microscopically, a section of the cyst wall revealed one surface lined with mesothelial cells and the opposing surface lined with endothelial cells. Numerous large dilated lymph channels were present in the wall and there were a moderate number of small blood vessels. The stroma was a loose network of collagen and elastic fibers. Small areas were composed of fat cells. The diagnosis was lymphatic cyst of the omentum.

FIG. 1. Photograph of omental cyst.

SUMMARY

A case of an unusually large omental cyst weighing 2,600 gm. is reported in a four year old girl. The diagnosis was made preoperatively and excision was accomplished.

REFERENCES

1. GROSS, R. E. The Surgery of Infancy and Childhood, pp. 377. Philadelphia, 1953. W. B. Saunders Co.
2. ARATA, J. E. and BLANCHET, H. J. Large primary omental cyst simulating acute appendicitis. *Armed Forces M. J.*, 5: 536–539, 1954.

A New Non-crushing Clamp for Gastrointestinal Surgery

PETER K. WASKO, M.D., *Perth Amboy, New Jersey*

From the Department of Surgery, General Hospital, Perth Amboy, New Jersey.

MANY surgeons have tried to prevent the tissue trauma which occurs during operation due to crushing instruments. Rubber tubing has been used over the jaws of the clamps, but rubber-covered instruments have not been completely satisfactory for the following reasons: (1) Most instruments used have been straight or curved to a certain degree. The straight clamp and the curved clamp never give parallel and equal clamping surface. (2) The closing action of the metallic jaws is not limited and the contact of the two clamping surfaces, even though covered with rubber, can produce trauma to the tissue. (3) Usually the metallic jaws have been flat and broad, thus creating an extensive clamping surface which increases the chances of traumatic injuries. (4) Rubber tubing used as protective covering has not been anchored tightly to the instrument and slipping has often occurred. (5) The clamping surface of the rubber tubing has usually been smooth so that a slipping tendency is created. (6) The type of rubber tubing used is not entirely satisfactory to avoid tissue injury. (7) Difficulty is often encountered in the placing of the clamp in an area where space is limited.

For a long time there has been a need for an adequate parallel, non-crushing, non-tearing instrument which can be delicately tightened. In order to permit this surgical approach a special clamp has been devised. The instrument with double lumen rubber tubing shown in Figures 1 and 2 has been designed to insure minimal tissue trauma. The clamp consists of parallel round metallic jaws positioned at 90 degrees to the handle. The double lumen rubber tube covering the metallic jaws produces an instrument which in effect is similar to the human finger, with the round metallic jaw simulating bone and the rubber tubing corresponding to the soft tissue.

This clamp has the following advantages: (1) The 90 degree angle between the jaw and handle of the clamp assures parallel and equal clamping force of the jaws. Experimentation has proved that this is the only angle at which this is possible. (2) The closing action of the metallic jaws is limited to a certain extent so as to prevent contact of the metallic jaws and injury to the tissue. (3) The clamp has round jaws about 3 mm. in diameter which decrease the clamping surface to a minimum and proportionally increase the supporting surface of the rubber tubing. (4) The round metallic jaws of the clamp are inserted into the small lumen of the rubber tube. Due to difference in diameter and the high elasticity of the rubber, the tube covering remains securely in place. (5) The clamping surface of the rubber tubing has a longitudinal groove sufficient to minimize slipping. This arrangement allows the jaws to slide easily into place without rolling the bowel. (6) The rubber tubing consists of double lumen: a larger lumen and a smaller one. The smaller lumen is about 1.5 mm. in diameter partially situated inside the wall of the external portion of the rubber tube; in such construction it permits a firm though gentle clamp, thus protecting the delicate tissue. (Fig. 3.) (7) With the right angle intestinal clamp it is much easier to clamp in an area in which space is limited, where the bowel cannot be mobilized sufficiently and where the bowel is too short to be brought to the surface for anastomosis. (8) The clamp is constructed in such a way that the jaws are fixed in a permanent position; therefore the tissue cannot slip in a sidewise direction. (9) The handle portion of the clamp

is curved to fall away from the operative area, thus providing freedom for the surgeon and facilitating surgery deep in the pelvis and abdomen. (10) The clamp is available in three sizes: The small size is suitable for duodenum and esophagus; the medium for small intestine and rectum; and the large size is often required for large bowel and stomach resection.

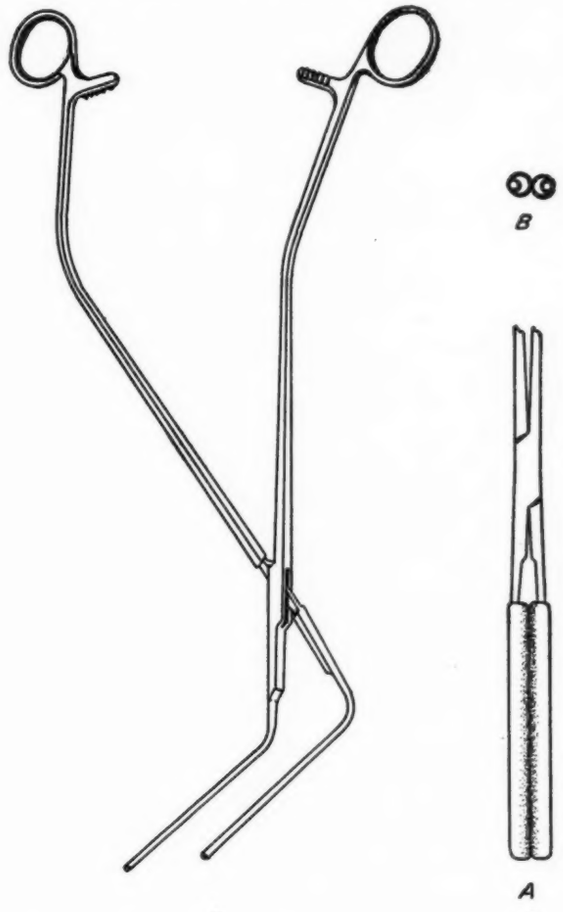


FIG. 1. Non-crushing clamp for gastrointestinal surgery. Drawing of the instrument which demonstrates the design more clearly.

FIG. 2. The metallic jaws of the clamp equipped with a double lumen rubber tube. A, front view of the clamp. B, side view of the clamp.

The clamp has been used in a number of cases including total and partial gastric resection, closure of duodenal stump, anastomosis of the esophagus with jejunum and with duodenum, and anastomosis of the small and large intestine end-to-end and side-to-side.

The new clamp permits rapid closure of the duodenum and anastomosis and eliminates the need of traction suture.

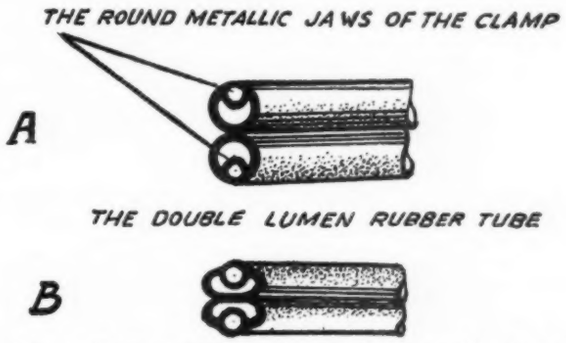


FIG. 3. Demonstration of double lumen rubber tube in action. A, the clamp has just been applied; the jaw of the clamp has not been tightened. In this position no significant pressure is exerted on the tissues. B, the jaws have been tightened sufficiently to occlude the lumen of the rubber tube and the capillary vessels; sufficient pressure is exerted to hold tissues in position without crushing and tearing.

There were no complications referable to the duodenal stump and to the anastomosis performed in this series of cases.

These successful operations are given indicating that the clamp was in place for one hour with no ill effects.

The design of this instrument employs the compressibility of both the elastic wall of the tubing and the inner larger lumen. The delicate control of tightening affords sufficient pressure to maintain the tissue between the double tubes without crushing and tearing. A gentle squeezing of the clamp has a tendency to diminish the amount of vascular oozing during surgery.

The author believes that the principles involved in this non-traumatic clamp should find great use among many other surgical fields such as cardiovascular, gynecologic and plastic surgery.

An Improved Sigmoidoscope for Operative Work

ALFRED L. SOLOW, M.D., *Boston, Massachusetts*

THIS report describes a new sigmoidoscope, compact in design, supplied with an easily manipulated suction tube and effective lighting system which allows either a proximal, distal or combination of both systems to be used. While it is an effective diagnostic instrument, it has found its greatest use in operative work.

The Sigmoidoscope Tube. The chromium-plated brass sigmoidoscope tube has a working length of 10 inches and a lumen ¾ inch in diameter. The outside diameter is approximately 13/16 inch. The distal opening is round with carefully machined, smooth, dull edges. The proximal opening is surrounded by a large flange flattened on two sides so that it may be rested on a table without rolling. The obturator is of the conventional type. (Fig. 1.)

The Lighting System. The lighting system employs a combined proximal and distal light, either of which may be used independently and yet provide an effective instrument. However, the instrument is most effective when both lights are used together, producing a maximum amount of well distributed light. This also insures adequate light should one or the other bulbs become blown or covered with fecal material. The distal light is located 1 inch from the end of the sigmoidoscope tube, avoiding the likelihood of accidental contact with a prolapsed intestine. It extends from a circular adapter which attaches to a lip in the proximal portion of the sigmoidoscope tube, positioning it flat along the bottom of the tube. The distal lamp has a spherical tip which affords a soft diffuse light and is not likely to pick up strands from a swab. The proximal light head is about 2.2 cm. in length. Made of chrome-plated brass, its distal lip is tapered so that it fits snugly into the distal light carrier. The proximal lamp protrudes slightly into the lumen and is provided with a lens cap, concentrating the light in a strongly focused beam. The back of the proximal light carrier is covered by a magnifying lens window which can be swung out of place while working, or in place for observation or air insufflation. The cords used are of two colors: (1) a black plastic-coated cord which attaches to the proximal light carrier and (2) a white one which attaches to the distal light. Except at the point of attachment to the light carriers, both cords are enclosed in a single plastic sleeve. They connect to the light carriers by a bayonet fitting which assures a firm contact. Each light operates from its own current source. Although this makes two current sources necessary, it also assures adequate lighting under almost any circumstances. The purpose of the two-color cords is to allow the operator to know which light system is being controlled at a given time. (Fig. 2.)

Suction Tube. The suction tip and smoke evacuator is a long, slender, metal tube with multiple small perforations at its distal end. The handle of the suction tip is widened and has an adapter which allows it to be held or fixed into the instrument by attaching to the proximal light carrier rim. We find that this apparatus provides adequate suction for evacuating thick mucus, liquid stool and blood. We also find that old discarded intravenous tubing makes a fine material to use as suction tubing for this instrument.

SUMMARY

We have described an improved sigmoidoscope with proximal and distal lighting, both operating off separate circuits, with an attachable suction apparatus which provides an efficient instrument for use in operative and diagnostic work and which will withstand heat sterilization.

* This instrument is manufactured by the National Electric Instrument Co., Inc., of Elmhurst, Long Island, N. Y.

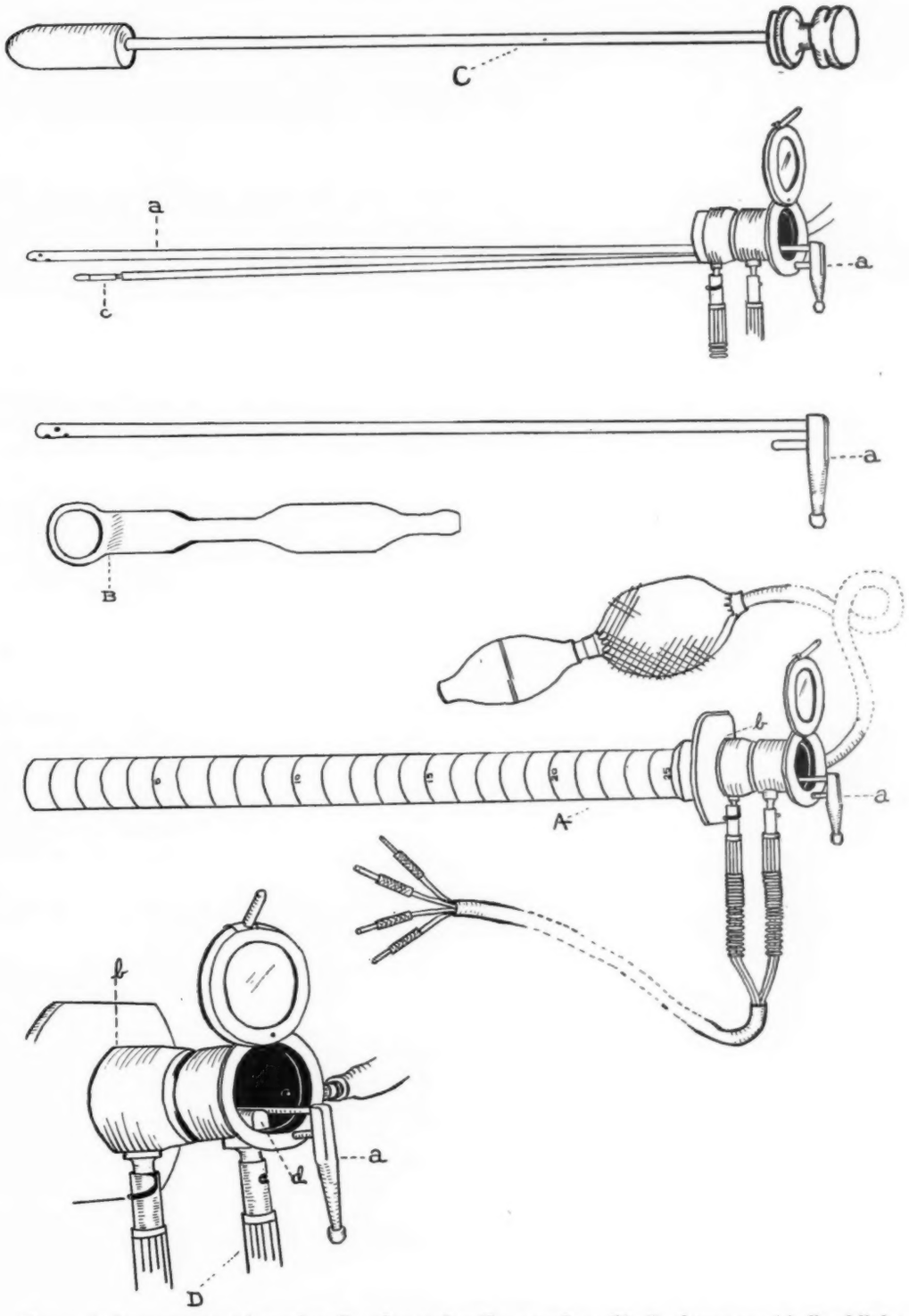


FIG. 1. A, instrument: (*a*) suction. B, adapter handle; attach at (*b*). C, obturator: (*c*) distal light; (*d*) proximal light. D, enlargement of instrument head.

FIG. 2. Light pattern.

Acknowledgments: We wish to thank Mr. H. S. Rubens, Director of Research for the National Electric Instrument Company, Inc.; Drs. E. T. Whitney and E. Parker Hayden for their suggestions; Mrs. Ellsworth, Operating Room Supervisor, New England Hospital, for sterilization studies; and Mrs. Charles Bowen for her sketches.

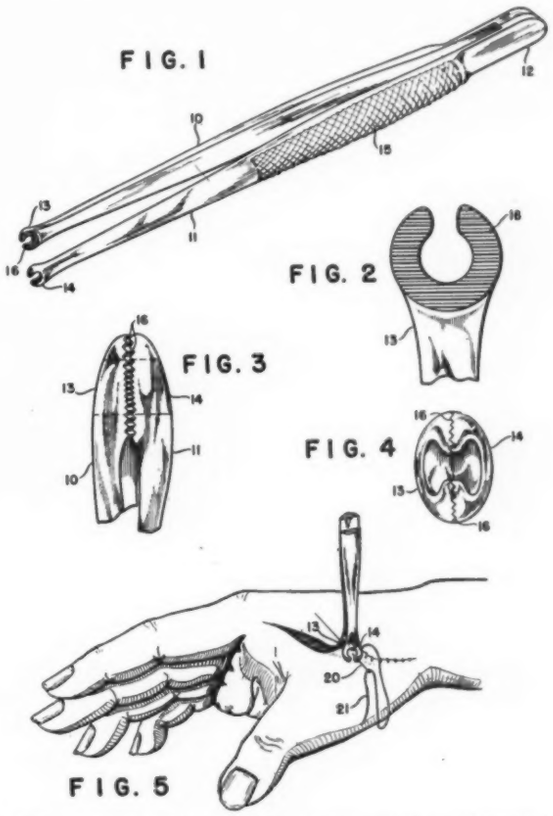
A New Suturing Forceps

F. A. L'ESPERANCE, M.D., *South Hadley Falls, Massachusetts*

As is well known, sutures used for closing incisions in the skin and other body tissues are normally applied by grasping the tissues to be joined together with a simple forceps. The suture is drawn through the tissue with a needle after piercing the flesh on opposite sides of the incision. The tissue is grasped with simple forceps to close the incision and to raise the tissue slightly as the needle is inserted *to one side of the point* picked up by the forceps. The needle may not pierce straight through the tissue but may skew to one side, thereby damaging a structure not meant to be sutured. Using ordinary forceps, the tissue may bend causing the suture to be placed at an angle. Again, if too much tension is used in placing the needle in the tissue, it may cut through and the suture pull out leaving a V-shaped tear along the incision edge, adding unnecessary trauma to the tissue. If one is working, for example, deep in and around the gallbladder area, picking the spot where the suture is to be placed with the forceps now in use is no guarantee that the needle will hit that spot. It may instead damage a nearby structure.

Accordingly, the primary object of the new suturing forceps is to overcome the foregoing disadvantages of the previous suturing forceps and methods. A more specific object of this invention is the production of an efficient forceps which will enable the average surgeon to suture an incision more quickly and efficiently. Still another object of the invention is the production of a simple forceps which will grasp tissue to be sutured in a dependable way, to locate accurately the spot to be sutured and to serve as a guide for the suturing needle. (Figs. 1 to 5.)

It is now evident that having located the exact spot to be sutured with this new suturing forceps one has only to place the needle into the C-shaped head of the jaws. This will insure that the needle is correctly placed and will go straight through the tissue, coming out of the C-shaped opening of the opposing jaw of the forceps. The needle cannot pull out, as the circular contour of the C-shaped head prevents this. It allows the suturing to be closer to the approximating edges of the wound without fear of the needle cutting through and the suture pulling out. Furthermore, by a centralization of the trauma of the forceps bite and the needle puncture into the same spot, one reduces considerably the trauma that would otherwise occur with the use of conventional type forceps.



FIGS. 1 to 5. The suturing forceps. Note: elongated arms (10, 11); serrated jaws (13, 14); knurled outer surface of arms (15); serrations on interior face of jaw (16); needle (20); suture (21).

In summary, the new suturing forceps provides a simple and dependable forceps for use in surgery. It allows better suturing than that afforded by forceps heretofore used and reduces the trauma which normally accompanies the suturing process. From the fine forceps of the eye or brain surgeon, the short forceps for skin suturing to the long forceps of abdominal surgery, definite advantages will readily be achieved with the use of this new forceps.

BOOK REVIEWS

Legal Medicine. Pathology and Toxicology. By Thomas A. Gonzales, M.D., Morgan Vance, M.D., Milton Helpern, M.D. and Charles J. Umberger, M.D. Introduction by Harrison S. Martland, M.D. Second edition, 1349 pages, 578 illustrations. New York, 1954. Appleton-Century-Crofts, Inc. *Price* $22.00.

One of our good friends was the late Dr. Harrison S. Martland, nationally known pathologist and Medical Examiner for Essex County, New Jersey. In the course of a conversation I told him I had an acquaintance who wrote Whodunit fiction and that this gentleman desired an up-to-date, authoritative work on forensic medicine. Harrison directed us to this work. Who would disagree with the scientific presentation of such eminent experts in this field? In our opinion, we deem our only task is to give a very brief résumé of what the book is about. The text presents the scientific methods and procedures used by the personnel of the Office of the Chief Medical Examiner in New York City for medical-legal investigation of deaths due to accidental or planned violence or poisoning, deaths due to natural but unknown causes or deaths which occur under suspicious circumstances. All of this is based on experience gained in the handling of more than 20,000 cases yearly. To continue, we cannot improve upon a further outline of this book which we read in a publisher's advertisement:

"It covers such a wide variety of subjects as investigation at the scene of death; identification; signs of death; the technic of autopsy; unexpected and sudden natural death; types and complications of trauma; blunt force injuries; stab wounds; bullet wounds; traumatic and gas asphyxia; thermic trauma; pregnancy; illegitimacy; abortion; infanticide; virginity; impotence; examinations of semen, blood, hair and other material; clinical examination for organic, inorganic and miscellaneous poisons; rights and obligations of physicians; malpractice; insanity; insurance and survivorship; and a technical section of analytic methods for determining the presence of and identification of various poisons."

No doubt this is the text or so-called Bible of most of the country's medical examiners. Should there be any of these gentlemen who are not familiar with this work or who do not own a copy, we urge them to purchase one at their very earliest convenience. All those scientifically bent, or who are Doctors of Medicine or engaged in any of the sidepaths of medicine will find this work instructive as well as absorbing reading. It is a scientific textbook on legal medicine, written by widely recognized top-notch experts, and well worth every penny of the price asked for it.

Textbook of Pediatrics. Edited by Waldo Nelson, M.D., with the collaboration of 70 contributors. Sixth edition, 1,581 pages, 438 figures. Philadelphia, 1954. W. B. Saunders Company.

We read in the Preface to the sixth edition: "This edition is a continuation of the Griffith, Griffith-Mitchell and Mitchell-Nelson series of Textbooks of Pediatrics. It is with personal regret that Dr. Mitchell's name is discontinued with this edition . . . I shall always think of future editions of the book in terms of the foundation laid by Dr. Griffith and by Dr. Mitchell."

This book needs no elaborate review. That it is now offered in a sixth edition and the fact that it has had a wide distribution speak for its value and high merit.

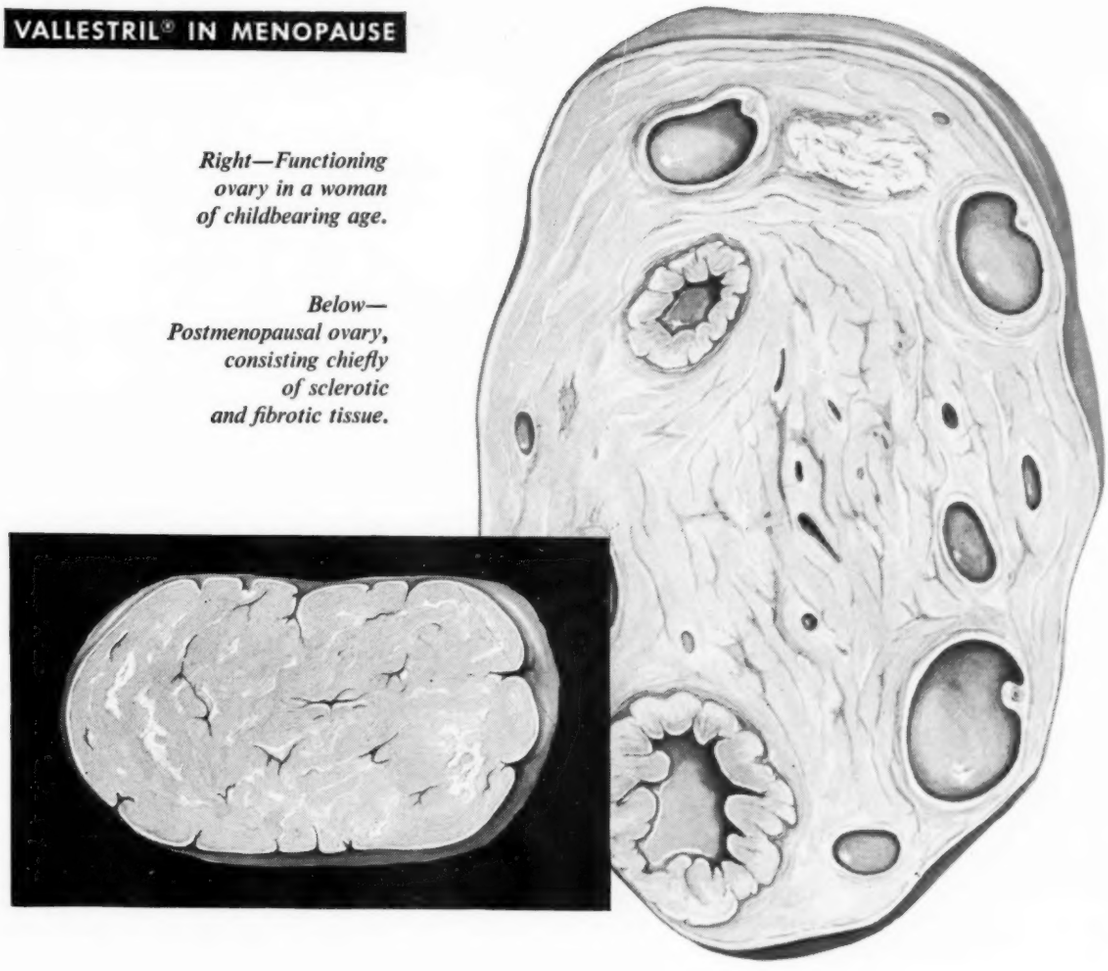
In this edition the intent was to make the text "as representative of current pediatric thought and practice as possible." This has been accomplished. Some sections have been completely rewritten, many largely so, and new sections and material have been added. The volume is up-to-date.

Naturally this work will appeal to students especially, and also to those interested in the medical care of children. However, the surgery of children plays an important role in modern medicine, and the surgeon who engages in this type of surgical practice will not be wasting his time in reading many parts of this monumental and outstanding collection of writings by the seventy specialists in this field.

VALLESTRIL® IN MENOPAUSE

Right—Functioning ovary in a woman of childbearing age.

Below—Postmenopausal ovary, consisting chiefly of sclerotic and fibrotic tissue.



"Target Action" in Estrogen Therapy

Vallestril is described as having "target action" because it provides potent estrogenic activity *only in certain organs.*

Vallestril combines a potent action on the *vaginal mucosa* with minimal effect on the *uterus or endometrium.*

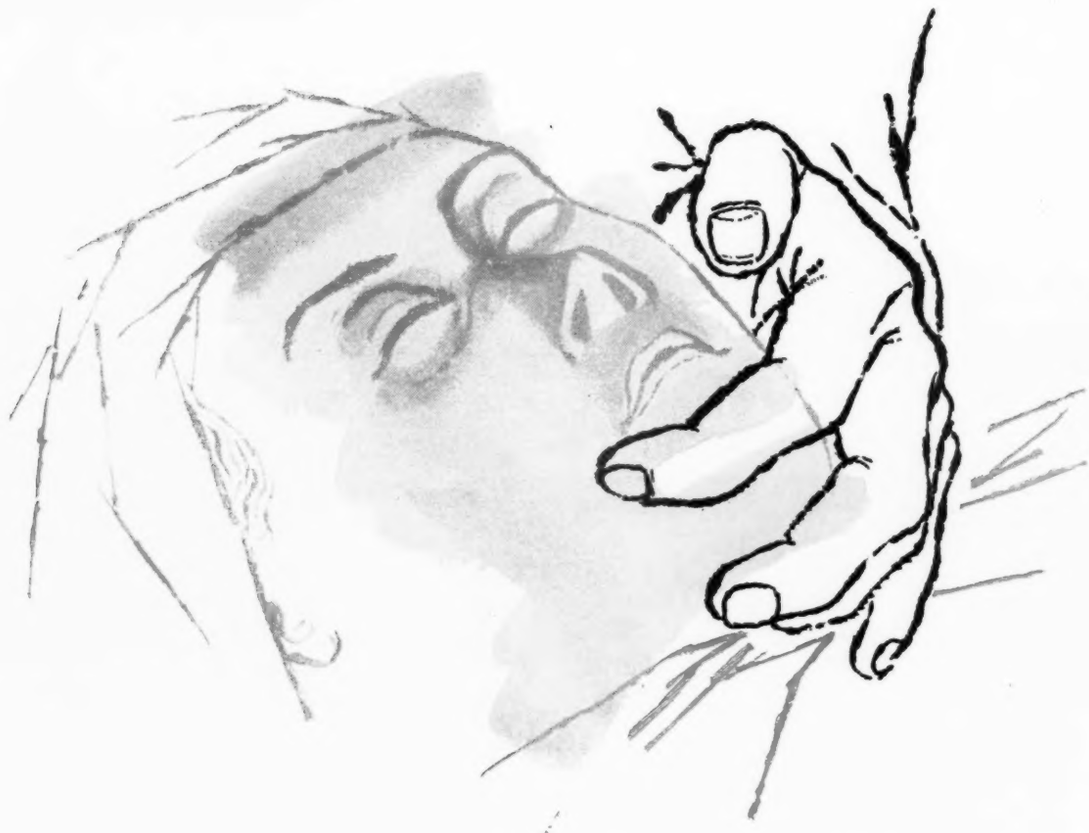
This distinctive, *selective* action helps explain the unusually low incidence of withdrawal bleeding as reported in recent carefully controlled studies. For this reason alone, Vallestril is preferentially indicated in the therapy of the menopausal syndrome.

Vallestril "quickly controls[1] menopausal symptoms, ... The beneficial effect of the medication appeared within three or four days in most menopausal patients. There is also evidence that the patient can be maintained in an asymptomatic state by a small daily dose, once the menopausal symptoms are controlled." The dosage in menopause is one tablet (3 mg.) two or three times daily for two or three weeks; then reduced to one or two tablets daily as long as required. G. D. Searle & Co., Research in the Service of Medicine.

---

[1]Sturnick, M. I., and Gargill, S. L.: Clinical Assay of a New Synthetic Estrogen: Vallestril, New England J. Med. *247*:829 (Nov. 27) 1952.

SEARLE



moment-to-moment control

PENTOTHAL® Sodium

(Sterile Thiopental Sodium, Abbott)

IN COMBINATION →

Quick response to the surgeon's needs
Reduced dosage of other agents
Compatibility with all other agents

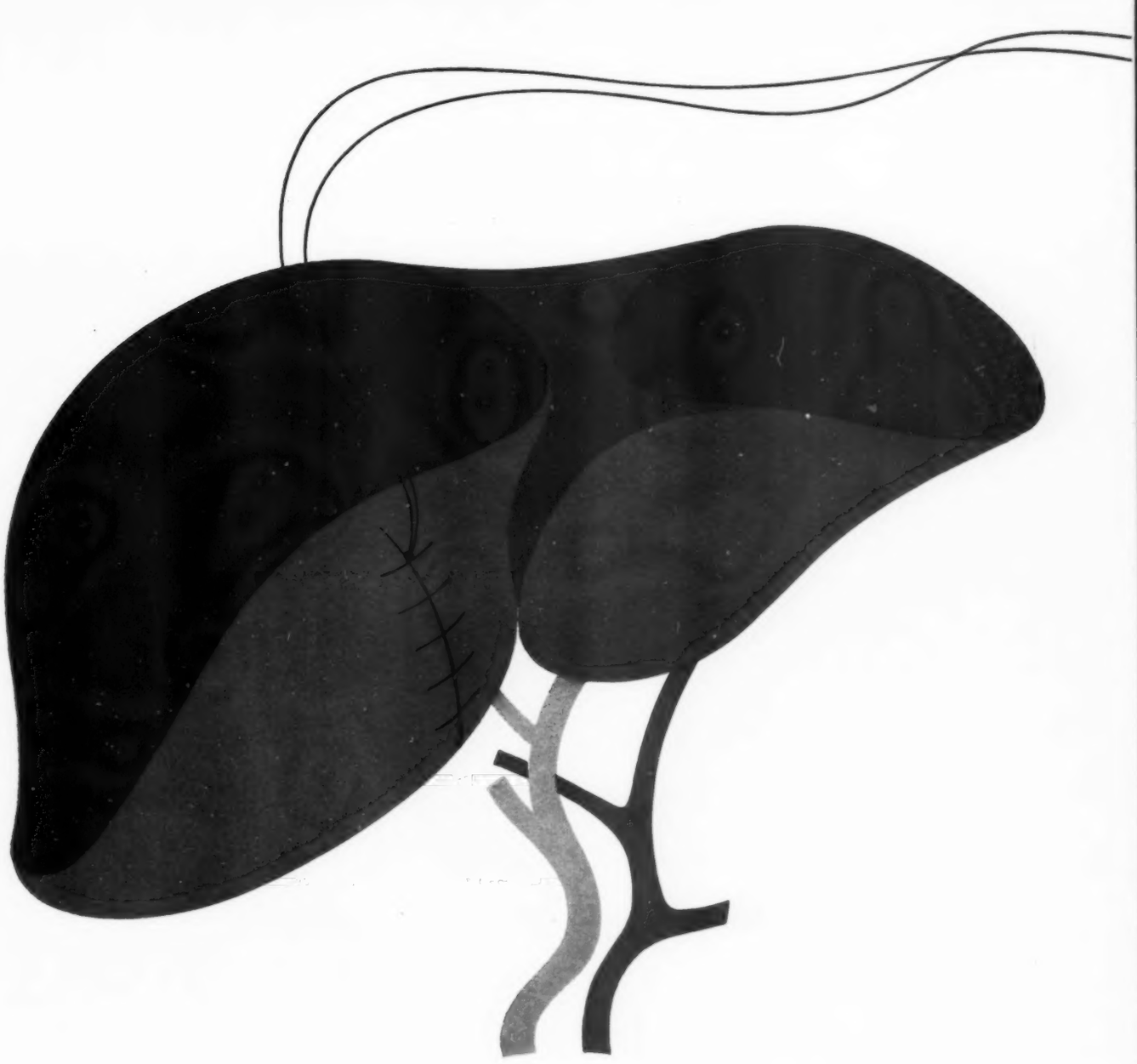
ALONE →

Easily-controlled levels
Rapid, smooth induction
Pleasant, swift recovery

→ Where PENTOTHAL is used frequently, enough solution to last from 24 to 48 hours may be prepared with assurance of stability. PENTOTHAL is now available in a 5-Gm. multiple-dose container (250-cc. size) and a 10-Gm. container (500-cc. size).

Abbott

503100



setting new standards

ETHICON®

sutures

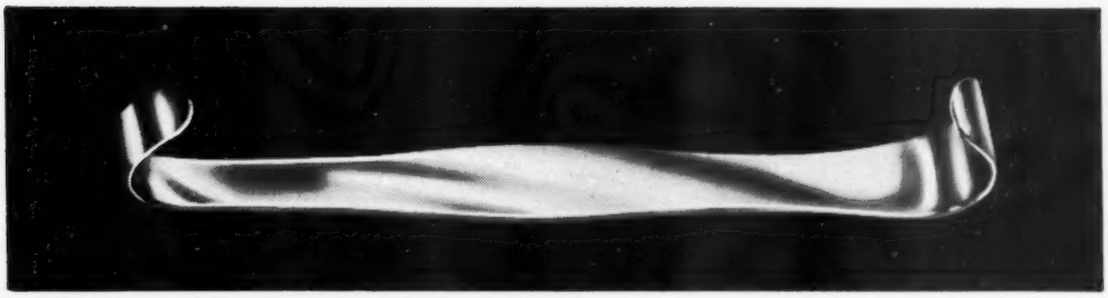
reverse cutting

ATRALOC NEEDLE SUTURES

20% more needle strength

ETHICON

ETHICON, INC.



Above, A TILLARY RETRACTOR OF POLISHED STAINLESS STEEL

Above, THE SAME RETRACTOR WITH THE NEW WECK G-P FINISH
Note the difference in glare!

new!

WECK G-P FINISH

—the Glare-Proof Finish for Surgical Instruments

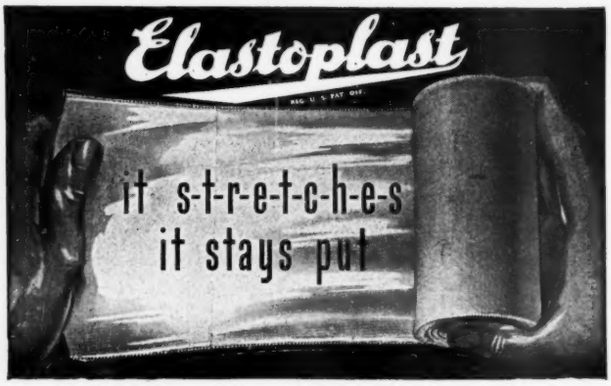
Even under normal conditions in the operating room, the glare of surgical instruments has been a problem. But with the development—especially in teaching hospitals—of the use of movie and television cameras requiring lights up to 16,000 watts—the problem becomes acute.

After many months of experimenting, Weck has produced a finish which tests have shown to be superior to the so-called "satin" and "black" finishes. This GLARE-PROOF finish has been achieved without sacrifice to the corrosion-resistant and ease of cleaning properties of the standard Weck stainless steel. Your inquiries are invited.

65 years of knowing how

EDWARD WECK & CO., INC.
135 JOHNSON ST., BROOKLYN 1, N. Y.

Manufacturers of Surgical Instruments • Hospital Supplies • Instrument Repairing



For
Comfort . . .
Neatness . .
For
Support . . .
Compression

The Dependable Original
E-L-A-S-T-I-C
Adhesive
Bandage

ELASTOPLAST

Trade Mark

Molds and holds to any contour . . . Allows joint motion . . . Provides firm support and controllable compression . . . Does not slip. Assures the neatest, most comfortable dressing in private and hospital practice. Available at your dealer in widths of 1, 2, 2½, 3, 4, 5 and 6 inches, 3 yards long (slack).

*** Elastoplast is also available in convenient unit dressings and compresses, Write for literature.**

DUKE LABORATORIES, INC.
STAMFORD, CONN.

Your valued hands, Doctor, *NEED*

Acid Mantle Creme

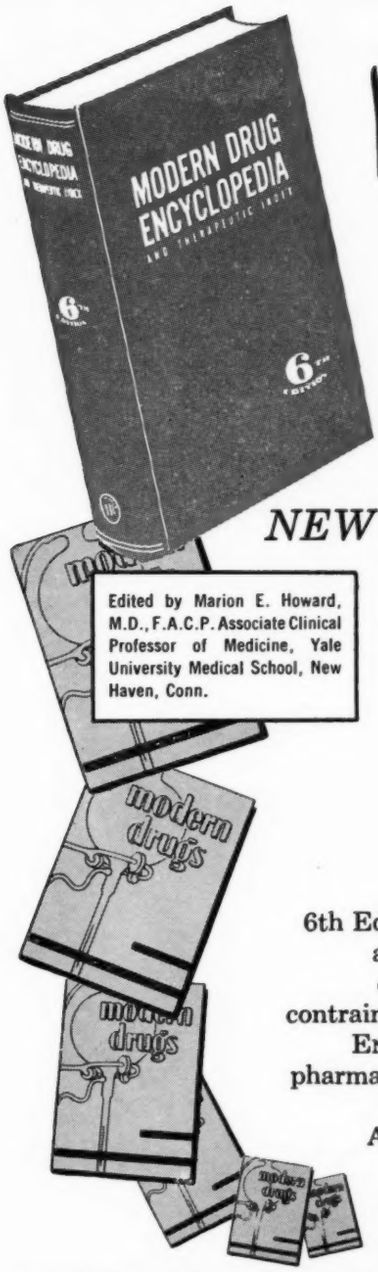
to prevent "surgeon's hands"

A Therapeutic—A Prophylactic
NOT a Barrier Cream

ACID MANTLE CREME—a buffered solution of aluminum acetate in a specially formulated hydrophilic base with a dermatologically correct pH of 4.2

For skin diseases in which there is an increased pH of the skin surface and/or a hypersensitivity to alkali, such as: Dermatitis of the hands in Surgeons, occupational Eczema due to primary irritants including soap and alkalis, Nummular Eczema, Bath Dermatitis, Winter Itch, Dry Skin and Seborrheic Dermatitis. *Write for Literature and Samples*

DOME CHEMICALS INC.
109 WEST 64th STREET, NEW YORK 23, N. Y.



Better than Ever...

for complete descriptions and authoritative data on nearly 4000 modern ethical drugs

NEW 6TH EDITION MODERN DRUG ENCYCLOPEDIA *and* THERAPEUTIC INDEX

Edited by Marion E. Howard, M.D., F.A.C.P. Associate Clinical Professor of Medicine, Yale University Medical School, New Haven, Conn.

with FREE Bi-monthly Supplement MODERN DRUGS to keep you up-to-date with newest ethical drug descriptions

The only three-year reference service of its kind with complete, authoritative data on new ethical drugs now completely revised in this new, "better than ever", 6th Edition. Prescription products, narcotics and exempt-narcotics are indicated for the first time. Here is your source for latest composition, action, uses, supply, dosage—also cautions and contraindications of thousands of new drugs. The MODERN DRUG ENCYCLOPEDIA is the leading finger-tip reference for physician, pharmacist, drug room and hospital infirmary, college and university. Compiled in seven special sections: DRUGS • BIOLOGICALS ALLERGENS • GENERIC NAME INDEX • THERAPEUTIC INDEX MANUFACTURER'S INDEX • GENERAL INDEX

HANDSOMELY BOUND IN RED FABRICOID, CONTAINS over 1500 PAGES, SIZE 6" x 9¼" x 2¼"

COMPLETE WITH GENERIC NAME INDEX AND SELF-PRONOUNCING DRUG LISTINGS

- ★ Over 50,000 Physician, Pharmacist, Institution users!
- ★ Now required reference by Michigan State Board of Pharmacy
- ★ Recognized as leading reference text by College and University Schools of Pharmacy
- ★ 97.2% subscribers who receive it . . . use it
- ★ 89.8% keep it within finger-tip reach

MAIL THIS COUPON NOW

DRUG PUBLICATIONS, INC.
49 West 45th Street, New York 36, N. Y.

Enclosed is the sum of fifteen dollars ($15.00** U.S.A.) for which please send me postpaid the Sixth Edition of the MODERN DRUG ENCYCLOPEDIA AND THERAPEUTIC INDEX plus the bi-monthly supplementary service, MODERN DRUGS.

NAME_____

ADDRESS_____

CITY_____ ZONE____ STATE_____

**Foreign $18.00 **Includes three-year supplementary service at $3 per year.

in keeping with your professional standards . . .

NO HALFWAY MEASURES IN SURGERY

WITH

Diaparene® CHLORIDE

SURGICAL SOLUTION

(A PRE-AUTOCLAVE ANTISEPTIC RINSE)

In a comparative control study, preautoclaved antibacterial rinsing of surgical caps and gowns with Diaparene Chloride (1:5000), a non-volatile antiseptic, prevented contamination of the operative field by the passage of bacteria through surgical linen wet from perspiration in 89% of the cases tested. Neither toxic nor allergic reactions were noted. Recommended usage: four ounces per 100 lbs. dry weight; supplied in 5 gallon carboys.

•

The Surgical Linen Division of many Diaparene diaper services (check classified phone book) offers preautoclave rinsing with Diaparene Chloride as an approved hospital service.

1 Collette, T.S.: Editorial—False Faith in the Surgeon's Gown and Surgical Drape: Am. J. Surg., 83:125-126, 1952.
2. Propst, H.D.: The Effect of Bactericidal Agents on the Sterility of Surgical Linen: Am. J. Surg. 86:301-308, 1953.
3. Colebrook, L. and Hood, A.M.: Infection Through Soaked Dressings: Lancet, 2:682, 1948.
4. Silverstein, M.E., New York City, N.Y., Personal Communication, November 10, 1952.
5. Baker, E., Madden, J.L. and Hartz, M., New York City, N.Y., Personal Communication, November 29, 1954.

Professional samples and literature available on antibacterial Diaparene Chloride Surgical Solution, dusting powder, lotion, water-miscible ointment and water-repellent creme.

PHARMACEUTICAL DIVISION, HOMEMAKERS' PRODUCTS CORPORATION • NEW YORK 10, NEW YORK • TORONTO 10, CANADA

Convenient! Complete!

TUBE-FEEDING FORMULA supplies essential nutrients for 24 hours!

MIX:

1 qt. whole milk

3 cups (405 Gm.) non-fat milk powder

4 heaping tbsps. (60 Gm.) GEVRAL PROTEIN

Water to make 2,000 cc.

SUPPLIES:

Liquid	2,000 cc.
Protein	217 Gm.
Fat	42 Gm.
Carbohydrate	273 Gm.
Calories	2,354

Lederle

GEVRAL* PROTEIN

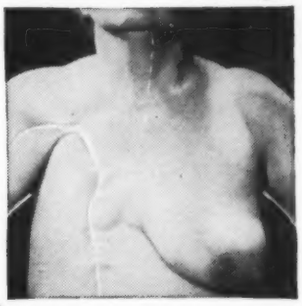
Geriatric Vitamin-Mineral-Protein Supplement Lederle

LEDERLE LABORATORIES DIVISION

AMERICAN Cyanamid COMPANY Pearl River, New York

*REG. U.S. PAT. OFF.

after Mastectomy



only

IDENTICAL® form

a "surprisingly simple"

breast form

restores Normal Contour
Natural Alignment
Life-like Motion
Self Confidence

through balancing weight compensation and natural fluidity of motion

adaptable to any brassiere, even bathing suit

Recommended by leading doctors because of its excellent cosmetic results and its ability to meet the patient's previously overlooked physiological needs.

Available in 24 sizes. Expertly fitted in leading stores throughout the United States and Canada

Patented U.S.A. & Foreign Countries

ACCEPTED FOR ADVERTISING IN PUBLICATIONS OF THE AMERICAN MEDICAL ASSOCIATION

IDENTICAL FORM, INC.
17 West 60 St., New York 23, N.Y.

Please send professional literature and list of authorized dealers.

_____ M.D.

Address _____

City _____ Zone _____ State _____ JS

COOK COUNTY
GRADUATE SCHOOL OF MEDICINE

INTENSIVE POSTGRADUATE COURSES

STARTING DATES, SPRING 1955

SURGERY—Surgical Technic, Two Weeks, April 4, April 18
Surgical Technic, Surgical Anatomy & Clinical Surgery, Four Weeks, June 6
Surgical Anatomy & Clinical Surgery, Two Weeks, March 21
Surgery of Colon & Rectum, One Week, April 11
Basic Principles in General Surgery, Two Weeks, March 28
General Surgery, Two Weeks, April 25; One Week, May 23
Gallbladder Surgery, Ten Hours, April 11
Fractures & Traumatic Surgery, Two Weeks, June 13

GYNECOLOGY—Office & Operative Gynecology, Two Weeks, April 18
Vaginal Approach to Pelvic Surgery, One Week, May 2

OBSTETRICS—General & Surgical Obstetrics, Two Weeks, March 28

MEDICINE—Two-Week Course May 2
Electrocardiography & Heart Disease, Two Weeks, July 11
Gastroenterology, Two Weeks, May 16
Dermatology, Two Weeks, May 9
Hematology, One Week, June 13

RADIOLOGY—Diagnostic Course, Two Weeks, May 2
Clinical Uses of Radio Isotopes, Two Weeks, May 2
Radium Therapy, One Week, May 23

PEDIATRICS—Intensive Course, Two Weeks, April 4
Clinical Course, Two Weeks, by appointment
Cerebral Palsy, Two Weeks, June 20

UROLOGY—Two-Week Urology Course, April 18
Ten-Day Practical Course in Cystoscopy every two weeks

TEACHING FACULTY—ATTENDING STAFF
of Cook County Hospital

Address Registrar, **707 South Wood Street, Chicago 12, Illinois**

THE NEW YORK POLYCLINIC
MEDICAL SCHOOL AND HOSPITAL

(ORGANIZED 1881)

(The Pioneer Post-Graduate Medical Institution in America)

SURGERY & ALLIED SUBJECTS

A two months full time combined surgical course comprising general surgery, traumatic surgery, abdominal surgery, gastroenterology, proctology, gynecological surgery, urological surgery. Attendance at lectures, witnessing operations, examination of patients preoperatively and postoperatively, and follow-up in the wards postoperatively. Pathology, radiology, physical medicine, anesthesia. Cadaver demonstrations in surgical anatomy, thoracic surgery, proctology, orthopedics. Operative surgery and operative gynecology on the cadaver; attendance at departmental and general conferences.

RADIOLOGY

A comprehensive review of the physics and higher mathematics involved, film interpretation, all standard general roentgen diagnostic procedures, methods of application and doses of radiation therapy, both x-ray and radium, standard and special fluoroscopic procedures. A review of dermatological lesions and tumors susceptible to roentgen therapy is given, together with methods and dosage calculation of treatments. Special attention is given to the newer diagnostic methods associated with the employment of contrast media, such as bronchography with Lipiodol, uterosalpingography, visualization of cardiac chambers, peri-renal insufflation and myelography. Discussions covering roentgen departmental management are also included.

EYE, EAR, NOSE and THROAT

A combined full-time course covering an academic year (9 months). It consists of attendance at clinics, witnessing operations, lectures, demonstration of cases and cadaver demonstrations; operative eye, ear, nose and throat (cadaver); head and neck dissection (cadaver); clinical and cadaver demonstrations in bronchoscopy, laryngeal surgery and surgery for facial palsy; refraction; radiology; pathology; bacteriology; embryology; physiology; neuro-anatomy; anesthesia; physical medicine; allergy; examination of patients pre-operatively and follow-up post-operatively in the wards and clinics. Also refresher courses (3 months).

COURSE FOR GENERAL PRACTITIONERS

Intensive full time instruction covering those subjects which are of particular interest to the physician in general practice. Fundamentals of the various medical and surgical specialties designed as a practical review of established procedures and recent advances in medicine and surgery. Subjects related to general medicine are covered and the surgical departments participate in giving fundamental instruction in their specialties. Pathology and radiology are included. The class is expected to attend departmental and general conferences.

FOR INFORMATION ABOUT THESE AND OTHER COURSES ADDRESS

THE DEAN, 345 West 50th Street, NEW YORK 19, N. Y.

Precision
FOR INCISION

As the "Master Blade" for the Master Hand, where the need is for PRECISION, every Crescent Blade is precision-made for fine balance . . . precision-honed for extreme sharpness . . . precision-tested for strength and rigidity.

Precision-performance is assured by the new Swedish steel of high carbon content and unusually fine grain.

Precision-protection is provided by the new moisture-proof, all-climate, aluminum-foil wrapping.

Samples on request

CRESCENT SURGICAL SALES CO., INC.
48-41 Van Dam Street, Long Island City, New York

Crescent

SURGICAL BLADES AND HANDLES

Back Issues Wanted

(MUST BE IN PERFECT CONDITION)

THE AMERICAN JOURNAL OF SURGERY

will pay

$1.00 per copy for the following issues:

March 1952
April 1952
May 1952
November 1, 1950
January 1950

Send to

THE AMERICAN JOURNAL OF SURGERY, Inc.
49 West 45th Street
New York 36, N. Y.

NOTES AND QUOTES

An extensive analysis of the American Medical Association by the student editors of the Yale Law Journal criticizes the A.M.A.'s excessive authority over medical practice and its failure to use this power as an "instrument of progress." The eighty-four-page report, published in a recent issue of the Yale Law Journal, contains both criticism and praise for the A.M.A., but the criticisms predominate. The editors' conclusions, reached after nearly two years of research, are based upon studies of the A.M.A.'s published records, interviews with both its critics and proponents and a questionnaire directed to state medical societies.

In Chicago Dr. George F. Lull, Secretary and General Manager of the American Medical Association, who received an advance copy of the article shortly before it went to press, issued a strong statement in answer to the article. "It took the students two years to make the study, but they took neither the time nor the trouble to interview A.M.A. officers or staff people at the Chicago headquarters to get their facts correct.

"It is most unfortunate that the article was submitted to us so late that insufficient time remained before publication for correction of basic and glaring errors of fact and omissions of vital facts. In many important sections the text is based on completely false and erroneous information," he said.

The Yale Law Journal article finds that "no other voluntary association commands such power within its area of interests as does the A.M.A. It holds a position of authority over the individual doctor, wields a determining voice in medical education, controls the conditions of practice, and occupies a unique position of influence in shaping government health policies."

For example, the authors charge that the A.M.A.'s power has been used to block virtually all plans for providing low-cost health and medical care unless subjected to Medical Society control. At present, the article continues, the A.M.A. is opposing President Eisenhower's proposal for federal government reinsurance of voluntary health plans on the thesis that this might lead to socialized medicine.

In rebuttal to this statement Dr. Lull said that "the American Medical Association opposed the federal reinsurance plan because it was unnecessary and represents the intrusion of the federal government into a phenomenally successful area of private enterprise. Evidently the House of Representatives felt the same way because it recently 'killed' the bill by an overwhelming majority—238 to 134."

The Yale Law Journal pointed out that although many physicians are critical of A.M.A. policies, the A.M.A., with its total national income of $9,000,000 a year, is not truly representative of the nation's doctors and does not tolerate conflicting opinions within its membership. The article claims further that the J.A.M.A. "rarely prints opinions in disagreement with positions taken by the organization's governing boards."

Dr. Lull branded this statement as false. "On the contrary, the A.M.A. is so representative of its membership that many other organizations, including the American Bar Association, have modeled their organizational structure after the A.M.A."

Doctors who defy A.M.A. authority, the Yale law students argue, may be subjected to professional ostracism, which could cut them off from patient referrals and consultations, deny them advancement in hospitals, or bar them from professional appointments.

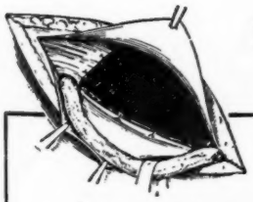
Dr. Lull also branded this statement as false. "The American Medical Association has almost no authority over individual physicians. It is the county medical society that disciplines members who are guilty of unethical practices."

In his concluding statement of rebuttal to the student article Dr. Lull said: "The real danger in this article is that nearly all of the facts are given a negative slant whereas they just as well could have been presented in a positive light. It is very apparent that the authors built up a straw man and then proceeded to knock him down. It is an obvious attempt to neutralize the conservative influence of one of America's great voluntary health organizations."

DR. ALTON OCHSNER, William Henderson Professor of Surgery and Chairman of the Department of Surgery in the Tulane University School of Medicine, has received the 1955 Modern Medicine award.

Dr. Walter C. Alvarez said the award was

CONTINUED ON PAGE 44



United FOUNDATION WIRE MESH
STAINLESS STEEL

NON-FRAGMENTING
NON-IRRITATING
NON-MAGNETIC

8 Different WEAVES for Permanent REPAIR of DIFFICULT HERNIAS, BONES, CARTILAGE, ARTERIES and TISSUES

Write Dept. M for Literature and Samples

United SURGICAL SUPPLIES CO.
650 Halstead Ave., Mamaroneck, N. Y.

For the finest SPECIALTY instruments
CHECK WITH COCHRANE

James F. Best, Pres.

DEPENDABLE QUALITY SERVICE

L. W. McHugh, V. Pres.-Treas.

COCHRANE PHYSICIANS' SUPPLIES, Inc.
133 EAST 58th STREET . NEW YORK 22, N.Y.
PHONE—PLaza 3-5533, 3-5534, 3-5491

Disintegrating

ALESEN T-TUBE

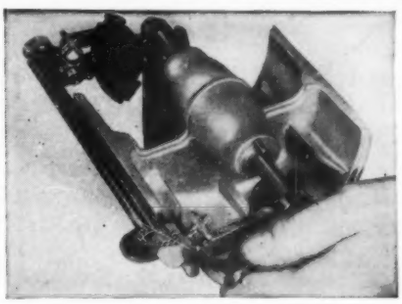
For Safer Gastrectomy

Reduces hazard of duodeno. stump disruption. Smoother post-operative convalescence. Disintegrates and discharged in 5 to 7 days post-operatively. Contains barium sulfate for x-ray purposes. Available at your Surgical Supply House.

Write for Literature

SEAL-INS LABORATORIES
2857 East 11th Street, Los Angeles 23, Calif.

The Improved



PADGETT-HOOD DERMATOME

For simplified split skin grafting with real accuracy and speed

➡ Inexpensive **THROW-AWAY** blades

➡ **DERMATOME TAPE** available for all models

Write for complete catalog today

KANSAS CITY ASSEMBLAGE CO.
816 Locust Street Kansas City, Missouri

ILEOSTOMY BAGS
Custom Built to Order

•

CEMENTED TO THE SKIN
LEAK PROOF

•

H. W. RUTZEN & SON
Surgical Appliances—Dept. S.
3451 West Irving Park,
Chicago 18, Illinois

Swivel
WALKING BUTTON

Swivel Action
Self Leveling
Renewable Tips
Neat, Trim Casts

$2.75 each order today

No torsion strain

THE TOWER COMPANY, INC. - P. O. BOX 3181 - SEATTLE 14, WASHINGTON

RADIUM
RADON

SEEDS — APPLICATORS

THE RADIUM EMANATION CORP.
GRAYBAR BUILDING, NEW YORK 17, N. Y.
MURRAY HILL 3-8636

given to Dr. Ochsner for his "consistent record of thirty-five years of outstanding achievement in surgical treatment of cancer." Dr. Ochsner was one of the first to emphasize the possibility of cancer causing effects from cigarette smoking. He is a number of the National Lung Cancer Committee, a Director and former President of the American Cancer Society, and a leader in local, state and national cancer programs.

The Tulane professor is President of the International Society of Angiology and is the past president of many surgical societies, including the American College of Surgeons.

Nominations for the award are based on votes received from physicians throughout the United States.

A new development in needle and syringe sterilizing bags has been announced, the A.T.I. steriLine bag. It has a "built-in" sterilization indicator that changes color from white to black only under proper sterilizing conditions of time, steam and temperature. This new feature gives nurses and other hospital personnel the convenience of a bag plus the added assurance that its contents are sterile. Also, this new "steriLine indicator" eliminates all doubt and confusion in the sterilizing room, in storage and at the instant of use, as to which needles and syringes have been autoclaved, and which have not.

Patent application on this bag has been made by the Aseptic-Thermo Indicator Company. The bag has been under close laboratory study for more than a year and has been tested in actual use in twenty-one major hospitals. It is stated that the "built-in" indicator is a dependable method for determining if the contents and the bag have been subjected to sterilizing conditions. This new feature, plus the fact that the bag is a time and labor saver, is a big advancement in hospital sterilization technics.

DePuy Manufacturing Company, Inc., Warsaw, Indiana, recently announced the introduction of the new DePuy Tip-Toe Splint by Ferciot. This splint was developed at the Lincoln Orthopaedic Center, Lincoln, Nebraska, by Dr. C. F. Fericiot who found that the severe flexion contracture of the ankles in the newborn frequently led to the development of calcaneal valgus deformity and pronated feet when the child began to walk.

Dr. Ferciot recommends correction of this tendency by use of the DePuy Tip-Toe Splint. This extension splint can be bandaged in the position of correction, and can be removed for bathing and exercise. Correction is usually obtained within four weeks.

These sturdy, well constructed splints are inexpensive, and immediately available. More information can be obtained by writing the manufacturer.

A new network television program which presents the latest news of advances in medical and pharmaceutical research was premiered in December over ABC-TV under the sponsorship of Ciba Pharmaceutical Products, Inc., Summit, N. J., with the cooperation of the American Medical Association.

Called "Horizons," the new program is a dramatic-documentary series designed for the physician and the interested layman audience. The narrator is Dr. Louis H. Bauer, past President of the American Medical Association, Secretary-General of the World Medical Association, and Chairman of the United Medical Service.

The risk of dying from heart and blood vessel diseases has gone up nearly 25 per cent among middle-aged men in the past generation, while the risk for women in the same age group has gone down by about the same amount. These opposite trends in the heart disease death rate of men and women between the ages of forty-five to sixty-five are the most striking piece of new information to be found in the 1954 revision of the statistical handbook, "Diseases of the Heart and Blood Vessels—Facts and Figures."

The sixteen-page booklet was prepared by the American Heart Association in cooperation with the National Heart Institute of the U. S. Public Health Service to present basic facts essential to an understanding of heart and blood vessel diseases as a major health problem. The revised booklet, containing thirteen charts and interpretive text, brings up to date the original edition of May, 1952.

CONTINUED ON PAGE 46

Freeman
BACK SUPPORTS

FREEMAN corset-type back supports are made in models which provide supportive and conservative measures in any required degree to almost complete immobilization. The great advantage of this type of garment is that it can be worn comfortably while sitting, standing or lying. Linings and stay covers are cushioned for comfort. All side-laced back supports have Freeman's exclusive self-smoothing, non-wrinkle fly.

Write for details of Freeman quality features and free pocket-size reference catalog.

FREEMAN MANUFACTURING CO.
DEPT. 902, STURGIS, MICHIGAN

The Primer Bandage (moist) and the Dalzoflex Bandage (elastic adhesive)—suggested in the Pressure Treatment of

LEG ULCERS, VARICOSITIES

and other ailments of the extremities where pressure is indicated. ***It Costs no more to use the best!***

Catalog and Prices on Request

Medical Aids Inc.

5 North Wabash Avenue Chicago 2, Illinois

Azochloramid®
Brand of CHLOROAZODIN U.S.P.
An Effective Anti-Bacterial Agent in
TRAUMATIC WOUNDS • DIABETIC GANGRENE
INFECTED ULCERS • DRAINING SINUSES

1935 ACCEPTED COUNCIL ON PHARMACY AND CHEMISTRY MEDICAL ASSOCIATION 1952

W&T Pharmaceutical Division

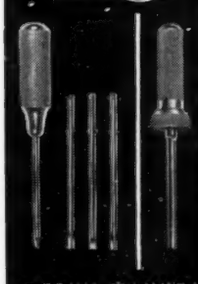
AZOCHLORAMID IN TRIACETIN 1:500
For moistening dressings and packings

AZOCHLORAMID SALINE MIXTURE
To prepare isotonic saline solution 1:3300 for irrigation, hot soaks, compresses, etc.

Non-toxic to tissue — Virtually non-irritating. Non-staining — Odorless — Strongly deodorizing PA-11

W&T WALLACE & TIERNAN PRODUCTS, INC., Belleville 9, N. J., U.S.A.

DePuy **SCREW DRIVER SET**



AND MASTER SCREW DRIVER

Screw Driver Set has four removable bits, one each single slot, Phillips, Woodruff, and cross slot. Bits easily inserted and removed. No. 565A, Aluminum Handle. No. 565S, Stainless Steel Handle.

Master Screw Driver has collet which grips screw tightly so it cannot drop. Screw is easily inserted, easily released. No. 378AS, Stainless Steel.

SEND FOR YOUR COPY OF FRACTURE APPLIANCES CATALOG.

our 60th year 1895 1955 DePuy

DEPUY MANUFACTURING CO., INC.
WARSAW 4, INDIANA

RADIUM
RADON

SEEDS — APPLICATORS

THE RADIUM EMANATION CORP.
GRAYBAR BUILDING, NEW YORK 17, N. Y.
MURRAY HILL 3-8636

NOTES AND QUOTES

Appointment of Dr. Robert C. Hockett as Associate Scientific Director of the Tobacco Industry Research Committee was announced recently by Dr. Clarence Cook Little, Scientific Director.

In his new capacity Dr. Hockett will assist Dr. Little and the Scientific Advisory Board in developing the tobacco industry's program of research into tobacco use and health. The Committee recently made initial grants totaling $82,000 *to six institutions for basic research projects, and is reviewing applications for additional grants.*

Dr. Hockett spent the nine years prior to 1952 *as Scientific Director of the Sugar Research Foundation. More recently he has been a consultant to Arthur D. Little, Inc., and to several pharmaceutical, food and beverage companies.*

A SPECIAL feature of the annual surgical "travel" clinic day of the Brooklyn-Long Island Chapter of the American College of Surgeons, held recently at St. Vincent's Hospital, was the televising of "live" operations as a part of the program.

For the first time medical color television added its dramatic close-up views to the scientific teaching activities of the clinic day. St. Vincent's is the only voluntary general hospital in the country equipped with permanent facilities which permit televising of operations directly from three of its major operating rooms to nine television screens located in the medical conference rooms and the auditorium. The television camera is installed in a cluster of surgical lights directly above each operating table and records every detail of the surgeon's progress graphically in color. The camera is controlled by an operator in a television control room adjacent to the operating room.

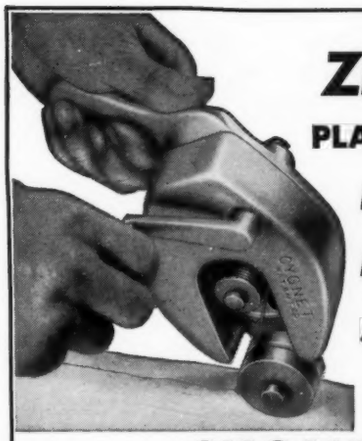
The practical benefits of this installation made the recent clinic of special interest to members of the American College of Surgeons. As the space-consuming area of the traditional viewing gallery is eliminated, the staff has complete freedom of action without concern over the ability of the audience to see what is going on in the operating field. St. Vincent's foresaw the advantages of such a permanent installation as one of the most valuable media in teaching surgery. Greatly magnified views were made possible by the addition of a 4½ inch by 6 inch video screen, supplied to St. Vincent's for the day through the courtesy of Smith, Kline and French Laboratories. The two operations televised were the excision of cataract and cancer of the thyroid with radical neck dissection.

A new rust and corrosion inhibitor for instrument disinfecting solutions is announced by the R. M. Hollingshead Corporation, Camden, New Jersey. The inhibitor prevents corrosion of metal instruments kept in liquid germicides and disinfectants which are usually highly corrosive. The new inhibitor, marketed as "Q.A.I.," is soluble in water base materials with a pH of 8.0 *or higher and is composed chemically of 2-hydroxypropylamine nitrite. The manufacturer claims that "Q.A.I." does not add to the toxicity of manufactured compounds and will not limit their germicidal properties. The inhibitor is incorporated directly into the manufactured product to be inhibited, and it will in turn prevent oxidation or rusting by any surface active agent. The addition of .05 per cent to 0.5 per cent "Q.A.I." will inhibit the corrosive properties of most products containing a quaternary ammonium compound in metal packages. A dilution of germicide containing .05% to* 0.1% *"Q.A.I." will prevent corrosion of metals placed in the germicide.*

ON February 10, 1955, the Buffalo Surgical Society sponsored the Roswell Park Lecture, this year given by Dr. Alfred Blalock, Professor and Director of the Department of Surgery, Johns Hopkins University. Dr. Blalock was awarded the society's Gold Medal given for the eighth time in honor of Dr. Roswell Park, Professor of Surgery at the University of Buffalo, 1883 through 1914. Previous lecturers and recipients of the medal were: Dr. Allen C. Whipple (1948), Dr. Evarts A. Graham (1949), Dr. Dallas B. Phemister (1950), Dr. Frederick A. Coller (1951), Dr. Edward D. Churchill (1952), Dr. Warren H. Cole (1953) and Dr. I. S. Ravdin (1954).

Americans with voluntary health insurance protection have passed the record-breaking 100 *million mark, it was reported recently by the Health Insurance Council, in announcing final*

CONTINUED ON PAGE 48



ZIP OFF
PLASTER CASTS
FASTER . . .
EASIER . . .
SAFER . . .
WITH

CYGNET
CAST REMOVER

NO DUST—NO NOISE—NO DANGER
USE IT ON ANY TYPE OF CAST

Cygnet pulls a stainless steel wire *thru* the cast, easily and cleanly. Entirely new approach to an old problem. If your dealer cannot supply Cygnet, have him write to us. If you want information we'll be glad to send you the whole story.

DUXE PRODUCTS
205-21 KEITH BLDG. CINCINNATI 2, OHIO

SERATURE "SPUR" WOUND CLIPS

★ *EASIER TO APPLY*
★ *EASIER TO REMOVE*
★ *LESS PAINFUL*

Serature "Spur" clips encourage better, faster healing with improved cosmetic results. Write for free clinical trial supply.

PROPPER MADE IN U.S.A. BY **MANUFACTURING COMPANY, INC.**
10–34 44th DRIVE LONG ISLAND CITY 1, N. Y.

THE NEW
Richards
ELECTRIC BONE DRILL AND SCREWDRIVER

Powerful, yet light weight. Easily controlled speeds for drilling or reaming. Cannulated head allows insertion of wires or Steinman pins. Sterilized by autoclaving.

RICHARDS MFG. CO., MEMPHIS, TENN.

For Comprehensive Emergency and Routine Burn Therapy

HEXATHRICIN
Aeropak (AUTOMATIC SPRAY)

Write for Professional Literature.

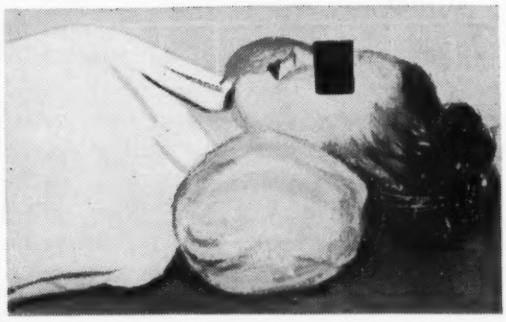
Lincoln LABORATORIES, INC.
P. O. BOX 1139 DECATUR, ILLINOIS

EXPLOSION-PROOF

Brown
Electro-Dermatome

Zimmer
MANUFACTURING CO., WARSAW, IND.

THE JACKSON CERVIPILLO ASSURES CORRECT SLEEPING POSTURE



Designed by Dr. Ruth Jackson to fit the normal contour of the neck and to relieve pain caused by irritation of the cervical nerve roots. In many instances this "Cervical Contour Pillow" has given relief of symptoms without any other treatment. Write for full details.

Distributed exclusively by:

LOUIS YELLIN, INC.
242 S. 17th STREET
Philadelphia 3, Pa.

NOTES AND QUOTES

results of its eighth annual survey on the extent of health insurance in the United States.

The Council reports for the close of 1953 a continuation of the "truly spectacular trends" of health insurance growth during the past decade, with more than 60 per cent of the total United States population now covered. "The survey shows," said Council Chairman John H. Miller, "that people today have more health insurance than ever before. And aggregate benefit payments have reached a new high, up sharply from the previous year. Altogether, the survey figures foretell continuing progress at rapid rates in the forseeable future."

RESEARCH grants of $150,000, advanced in 1954 to date, were announced by Dr. William R. Bond, Director of clinical research, A. H. Robins Co., Inc., Richmond, Va. The grants are awarded to laboratory and clinical researchers—largely in the field of internal medicine—in hospitals, medical schools and in private practice throughout the country.

In the treatment of chronic urinary tract infection following prostatectomy, nitrofurantoin (furadantin,® Eaton) "has been found to be highly effective," Drs. John W. Draper, Robert Zufall, Leon T. Rosenberg, and Vernon Knight state in reporting on forty-three elderly males, forty-two of whom had undergone prostatic operations. Prior to treatment the median urinary bacterial count of all patients was 1 million per ml. This was reduced to a median of 100 bacteria per ml. in the second week of treatment. The report, which appears in the Journal of Urology *(72: 1211, 1954), is from the Departments of Surgery and Medicine, Cornell Medical College and Bellevue Hospital, New York.*

The authors state that "treatment resulted in an abrupt fall in the number of bacteria in the urine, and, in almost one-half of the patients, sterile urines were obtained during treatment. The drug was most effective against infections with E. coli and B. proteus."

PASSING another milestone is the medical journal, Therapeutic Notes, which this year celebrates its sixtieth anniversary. Begun in 1894, the "parent edition" of this journal is sent by Parke, Davis & Company to approximately 175,000 physicians and allied professional people. Five other editions are published —British, Australian, Spanish, French and Portuguese—to give a worldwide circulation of 500,000 in every country outside the Iron Curtain. Originally printed in handbill style with large blocks of black type, Therapeutic Notes is now run off in four colors.

In "Facts about Mental Illness," The National Association for Mental Health, Inc., states the following:

1. *Today there are nearly three-quarters of a million people under the care of mental hospitals. This is more than half of the number of patients in all hospitals for all diseases in the entire country.*
2. *There are more people hospitalized for mental illness than for polio, cancer, heart disease, tuberculosis and all other diseases combined.*
3. *More than 250,000 new patients—one-quarter of a million—are admitted to mental hospitals each year.*
4. *In 1934 the chance of being hospitalized for a severe mental illness was computed as 1 in 20; today it is nearly 1 in 10.*
5. *At least ten million Americans—1 in every 16—are now suffering from some form of mental disorder.*
6. *During the past year some two and a half million men, women and children were treated for some form of mental disorder (in mental hospitals, at psychiatric clinics or in the offices of private psychiatrists).*
7. *Of the 19,000,000 who went to general hospitals last year to get treatment for physical ailments, at least 5,000,000 are estimated to have been suffering from some mental disturbance as well.*
8. *It is estimated that as many as 20 to 25 per cent of all employees in any corporation or industrial unit are suffering from mental disorders ranging from psychoses to "industrial maladjustment"—showing up in absenteeism, accidents, dissatisfaction, alcoholism, turnover, poor job performance.*
9. *More than half the patients in mental hospitals are suffering from schizophrenia. This means that more than one-fourth of all hospital beds are occupied by patients with schizophrenia.*

HEAD HALTER SET

complete as illustrated

adult	# 95A
youth	# 95B
child	# 95C

$9.00 per set

RAJOWALT CO.
ATWOOD, INDIANA
Sold only through Surgical Dealers

for your WORK, for your PLEASURE

you need the world's tiniest precision camera—the fabulous **minox**

so tiny (1⅛"x3¼"x⅝"), you always carry it. so light (2½ oz.), less than your keys.

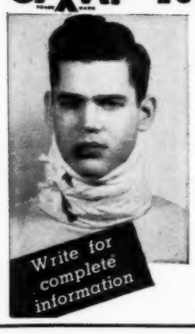
perfect candid pictures in black and white . . . and color. fast f/3.5 lens focuses as close as 8" and up to inf. all speeds from ½ sec. up to 1/1000 sec. *NO FLASH NECESSARY FOR INSIDE SHOTS. USE IN OPERATING ROOM and for CASE HISTORIES.* yields excellent large size prints.

minox III-S with chain and leather case **$139.50**

for literature—write Dept. D

KLING PHOTO CORP.
235 Fourth Avenue, New York 3, New York

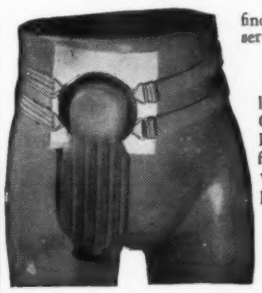
CAMP Lewin Cotton Collar



Simple, comfortable, effective therapeutic Cotton Collar. Exerts a protective, resilient, compressive and distractive force. Available at Camp dealers.

S. H. CAMP & COMPANY
Department A
Jackson, Michigan

Colostomy and Ileostomy Patients



find MORE convenience and LONGER service with

PERRY APPLIANCES

large variety of models and sizes CUPS, BAGS, PROTECTORS and IRRIGATORS, MANY FEATURES found ONLY in PERRY appliances. Write for folders showing complete line.

MURLE PERRY
3803 East Lake Street
Minneapolis 6, Minn.

new **ELASTICFOAM** TRADEMARK

the velvet-soft elastic bandage that stays in place like a second skin

ELASTICFOAM is a completely new type of bandage which combines the best properties of adhesive plaster, elastic, and cotton bandages. It is made by permanently bonding a sheet of multi-slit foam rubber to a superior quality cotton elastic bandage.

ELASTICFOAM stays in place like adhesive plaster—shaving is eliminated, redressing easy and painless.

Fully elastic (stretch 100%), does not narrow, maintains uniform pressure.

Velvet-soft and highly absorbent — may be applied directly over wounds, absorbs at least 5x its own weight of moisture.

ELASTICFOAM can be autoclaved. Economical — may be washed, sterilized and reused many times.

No allergic reactions reported after repeated application, does not mat under plaster casts nor interfere with X-ray.

knee, ankle, wrist, elbow, chest and back injuries

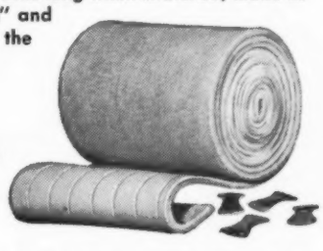
compression treatment of varicose veins, ulcers, phlebitis

postoperative dressings

in place of orthopedic felt

sports strapping—ankles, etc.

Elasticfoam bandages are 5 yards long when stretched, made in 2", 3", 4", 6", 8" widths, ⅛" and ¼" thicknesses. Available by the square yard for casts and other orthopedic work.



You must see and handle this unique bandage to appreciate its many advantages. Write for descriptive booklet and sample of Elasticfoam.

CONNECTICUT BANDAGE MILLS INC., 36 POLAND STREET, BRIDGEPORT, CONN.

FLAXEDIL*

Gallamine Triethiodide

(tri [diethylaminoethoxy] benzene triethyliodide)

LEDERLE

check-list of advantages in skeletal muscle relaxation

- ✓ Permits free manipulation of skeletal muscles and viscera.
- ✓ Requires less general anesthesia—speeds operative procedures.
- ✓ May be used to prevent fractures during electroshock therapy.
- ✓ Is readily miscible with thiopental solution.
- ✓ Relaxes spastic muscles during nonoperative orthopedic procedures.
- ✓ Is less toxic than d-tubocurarine—is quickly eliminated in the urine.
- ✓ Does not affect blood pressure significantly, nor cause sudden vascular collapse.
- ✓ Does not cause bronchospasm—possesses no histamine-like action.
- ✓ Does not affect parenchymal tissues, impede liver or kidney function.
- ✓ Does not cause vomiting nor affect the bowels.
- ✓ Can be used following administration of atropine or scopolamine.

Available in 10 cc. vials—20 mg. per cc. and 1 cc. ampuls—100 mg. per cc.

Lederle

*REG. U.S. PAT. OFF.

LEDERLE LABORATORIES DIVISION AMERICAN Cyanamid COMPANY
PEARL RIVER, NEW YORK

MARCH 1955

THE American JOURNAL OF Surgery

ADVERTISERS INDEX

Abbott Laboratories....16, 34
American Hospital Supply Corp.... 4
Ames Company, Inc.... 1
Austenal Laboratories, Inc.... 27
Ayerst Laboratories.... 8
Bard-Parker Co., Inc.... 30
Baxter Laboratories, Inc.... 4
S. H. Camp & Co.... 49
Ciba Pharmaceutical Products, Inc....
28, *Back Cover*
Cochrane Physicians' Supplies, Inc.... 43
Connecticut Bandage Mills, Inc.... 49
Cook County Grad. School of Medicine 40
Crescent Surgical Sales Co., Inc.... 41
Cutter Laboratories.... 6
DePuy Manufacturing Co.... 45
Doho Chemical Corp.... 17
Dome Chemicals, Inc.... 36
Duke Laboratories, Inc.... 36
Duxe Products.... 47
Ethicon Suture Laboratories, Inc....
Insert Facing Page 34
C. B. Fleet Co., Inc.... 24
Freeman Manufacturing Co.... 45
Gudebrod Bros. Silk Co., Inc.... 20
Hoffmann-LaRoche, Inc....
Insert Facing Page 24
Homemakers' Products Corporation... 38
Identical Form, Inc.... 39
Kansas City Assemblage Co.... 43
Kling Photo Corp.... 49
Lederle Laboratories....39, 50
Eli Lilly & Company.... 32
Lincoln Laboratories.... 47
The S. E. Massengill Co....
Insert Facing Page 16, 21
Medical Aids, Inc.... 45
V. Mueller & Co.... 10
National Electric Instrument Co., Inc.. 22
N.Y. Polyclinic Medical School & Hospital.... 40
Notes and Quotes....42, 44, 46, 48
Ortho Pharmaceutical Corporation.... 14
Parke, Davis & Co.... 19
Pfizer Laboratories, Div. of Chas. Pfizer & Co., Inc.... 25
Geo. P. Pilling & Son Co.... 12
Propper Mfg. Co.... 47
The Radium Emanation Corp....43, 45
Rajowalt Co.... 49
Riker Laboratories, Inc.... 13
Richards Mfg. Co., Inc.... 47
H. W. Rutzen & Son.... 43
Seal-Ins Laboratories, Inc.... 43
G. D. Searle & Co.... 33
Sharp & Dohme, Inc.... 26
E. R. Squibb & Sons, Div. of Mathieson Chemical Co.... 18
The Surgeon's Mart....43, 45, 47, 49
The Tower Co., Inc.... 43
United Surgical Supplies Co.... 43
The Upjohn Company....15, 23, 31
Wallace & Tiernan Products, Inc.... 45
Edward Weck & Co., Inc.... 35
Winthrop-Stearns, Inc.... 2
Louis Yellin, Inc.... 47
Zimmer Manufacturing Co.... 47

IN TENSION AND HYPERTENSION

sedation without hypnosis

℞ Serpasil T.M.

(reserpine CIBA)

A pure crystalline alkaloid of rauwolfia root
first identified, purified and introduced by CIBA

In anxiety, tension, nervousness and mild to severe neuroses—**as well as in hypertension**—SERPASIL provides a nonsoporific tranquilizing effect and a sense of well-being. Tablets, 0.25 mg. (scored) and 0.1 mg.

CIBA

SUMMIT, N.J.